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FIRST ANNUAL REPORT OF THE NATIONAL HEART AND LUNG ADVISORY COUNCIL

MESSAGE

FROM

THE PRESIDENT OF THE UNITED STATES

TRANSMITTING

THE FIRST ANNUAL REPORT OF THE NATIONAL HEART AND LUNG ADVISORY COUNCIL, PURSUANT TO SECTION 418(b)(2) OF PUBLIC LAW 92-423

JULY 29, 1974.—Message and accompanying papers referred to the Committee on Interstate and Foreign Commerce and ordered to be printed

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To the Congress of the United States:

I herewith transmit the First Annual Report of the National Heart and Lung Advisory Council, prepared in accordance with the requirement of Public Law 92-423, the "National Heart, Blood Vessel, Lung, and Blood Act of 1972."

It should be noted that funds for the Heart and Lung Institute have been increased greatly in recent years: from $195 million in 1971 to $286 million in 1974, to $309 million proposed for 1975. In short, the Administration's actions on the heart and lung program clearly identify it as an area of very high priority.

While there are recommendations in the Council's report that are at variance with the Administration's views, the Council's Report merits serious consideration and will be closely studied and evaluated. I am forwarding the report so that the Congress may also have it available for its deliberations.

RICHARD NIXON.

THE WHITE HOUSE, *July 29, 1974.*

FIRST ANNUAL REPORT OF THE NATIONAL HEART AND LUNG ADVISORY COUNCIL

SUBMITTED TO
THE PRESIDENT OF THE UNITED STATES
FOR TRANSMITTAL TO
THE CONGRESS OF THE UNITED STATES
IN ACCORDANCE WITH PUBLIC LAW 92-423

DECEMBER 17, 1973

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL HEART AND LUNG INSTITUTE
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Introduction

The members of the National Heart and Lung Advisory Council consider the following to be evident.

- Diseases of the heart, blood vessels, lungs, and blood cause more deaths among our people than all other diseases combined.
- The Congress and the President of the United States have expressed their desire and intent to increase the attack on the leading killer, heart disease, as well as on the next leading killer, cancer.
- An increased attack on diseases of the heart, blood vessels, lungs, and blood requires new knowledge; new understanding of the basic mechanisms that favor health or disease; new methods; new technical advances; better education for scientists, physicians, patients, and the public; and optimal utilization and application of existing knowledge.

To accomplish all that the Congress intended in the National Heart, Blood Vessel, Lung, and Blood Act of 1972 (Public Law 92-423), we must have the resources that the Congress authorized. These resources have not been forthcoming.

In this report, the Council recommends what is needed to achieve early diagnosis, effective treatment, and widespread prevention of diseases of the heart, blood vessels, lungs, and blood. To make our recommendations, we have reviewed and reevaluated our report of April 12, 1973 (Appendix A), and the summary of the National Heart, Blood Vessel, Lung, and Blood Program (Reference 1); we have examined the research and training now supported by the National Heart and Lung Institute; and we have considered recent changes in the policies of the Department of Health, Education, and Welfare and of the Office of Management and Budget that affect the accomplishment of the goals of the Congress and the President. Our report deals primarily with general mechanisms and policies. We have pointed out where we agree or disagree with present policies of the National Heart and Lung Institute, the National Institutes of Health, the Department of Health, Education, and Welfare, and the Office of Management and Budget.

This report of the National Heart and Lung Advisory Council is responsive to the requirement of Public Law 92-423 [Section 418(b)(2)] that the Council report annually on the progress of the National Heart, Blood Vessel, Lung, and Blood Program. When the National Heart and Lung Institute submitted its plan for the National Program to the Congress (Reference 1), the Acting Secretary of Health, Education, and Welfare, in his letter of transmittal (July 24, 1973), expressed his opinion that the value of the plan was limited by the "failure of the report to consider adequately the appropriate overall level for even the National Heart and Lung Institute in the context of the entire spectrum of biomedical research." The Council does not believe that it has responsibility for evaluating the needs of all biomedical research, nor did it attempt to do so. This Council does have the competence and responsibility to determine what the National Heart and Lung Institute needs to carry out its mission. The Council believes that it is the responsibility of the Congress and the Administration to determine the priority of this program in relation to other national needs.

We have not reiterated detailed progress in attaining the scientific priorities that we set in April 1973 (Appendix A) for specific research on heart, blood vessel, lung, and blood diseases because the most comprehensive review of the programs of the National Heart and Lung Institute in the history of the Institute was only recently conducted (1973). This review was accomplished by almost 250 medical and scientific advisors who composed 28 separate task groups within four panels established for heart and blood vessel diseases, lung diseases, blood diseases, and blood resources (References 2-6). The following are just a few examples of recent accomplishments and exciting new research.

- **Atherosclerosis** --the killer of most Americans--appears to be yielding to efforts such as surgery of blocked heart arteries, and the goal of preventing this disease has been brought closer by the discovery that atherosclerosis is associated with a focal increase in the numbers of smooth muscle cells in the inner lining of the arterial wall.

- **Respiratory distress syndrome** of infancy can now be predicted by simple diagnostic tests and, therefore, arrangements may be made to have the infant with this disorder born in special emergency-care centers where a new treatment[1]--continuous positive-airway-pressure--can be used to save the baby's life. A combination of basic research, clinical investigation, and emergency care has, within the past year, reduced the mortality from more than fifty percent to less than ten percent.

- **Echocardiography**, a new diagnostic technique, provides a safe, painless method for precisely locating defects within the beating heart that can be corrected surgically.

- **Sickle-cell disease** has been attacked through the development of a national program.

- **Heart defects in infants** can now be diagnosed and treated during the first few days of life, and this is saving many lives that would have been lost.

Major Conclusions, Recommendations, and Suggestions for Legislative Action

- The National Heart and Lung Advisory Council concludes that the most significant advances in the prevention and treatment of diseases of the heart, blood vessels, lungs, and blood will come from enhanced understanding of the underlying disease processes. For example, major gains in the prevention and treatment of atherosclerosis and its consequences--the nation's most prevalent and most serious health problem and one for which there is no effective treatment--are clearly dependent upon increasing our base of knowledge about this disease. The Council also concludes that the individual project grant, which supports the research of the innovative, creative, and imaginative scientist, is the most effective means of developing the necessary new information and ideas. The Council therefore emphasizes the urgent need to increase funds for research grants. We believe that the research grant programs of the National Heart and Lung Institute require approximately $141,000,000 in fiscal year 1974 and $176,000,000 in 1975. (Refer to recommended annual budgets, page 6.)

- In 1973, it became impossible to appoint a promising young scientist to a research traineeship or to nominate him for a postdoctoral fellowship. Legislation is therefore urgently required for assurance of an adequate number of research training programs and research fellowships to meet documented national needs. The Council believes that two mechanisms of support are needed immediately to replace those now being phased out: fellowships to support individuals who would benefit most by intensive research with a distinguished mentor in a special area, and training programs in highly qualified departments to support individuals who require interdisciplinary research training, such as young physicians who need broad scientific training or engineers, physicists, and mathematicians who are needed in research careers in the biomedical sciences. These training efforts will require $26,100,000 for the National Heart and Lung Institute in fiscal year 1975. (Refer to recommended annual budgets, page 6.)

- The Council recommends, as a very effective means of accomplishing national goals, that the National Heart and Lung Institute establish a stable Research Professorship in every medical school in the United States. Approximately $10,000,000 a year should be appropriated, and allocated, for this purpose. As another means of expanding the number of stable positions for creative scientists without diminishing the limited financial resources of universities and other research organizations, the Council also recommends that $15,000,000 a year be allocated to the National Heart and Lung Institute for the support of Professorial Research Groups, each of which would consist of several competent investigators. At least fifty of these units should be established at an average annual cost of approximately $300,000 for each group. (Refer to pages 11 and 12 and recommended annual budgets, page 6.)

- The Council urges that legislation be developed that would insure the continuation of the study section mechanism for review of scientific merit, as currently used by the National Institutes of Health, with appointment of members to these review groups based strictly on scientific expertise and demonstrated professional accomplishment. (Refer to pages 16 and 17.)

- The Council recommends that the procedures for appointment of the Director of the National Institutes of Health be thoroughly reviewed in congressional hearings and that legislation be enacted that would make the appointment by the President subject to the advice and consent of the Senate. The Council also recommends that an Inter-Council Advisory Committee of the National Institutes of Health be given the opportunity to make recommendations to the President with respect to such appointment. (Refer to pages 21 and 22.)

- The Council places a very high priority on the construction of research facilities. The previous report of the Council (Appendix A) and the National Heart, Blood Vessel, Lung, and Blood Act of 1972 both call for National Research and Demonstration Centers; in addition, the Council's report calls for support of more than a hundred Research Professors and fifty Professorial Research Groups and for an expansion of research efforts. All of these objectives will need additional research laboratories at an initial cost of $60,000,000. (Refer to pages 19-20 and recommended annual budgets, page 6.)

- The Council recommends that legislation be enacted that would establish minimal qualifications for appointment to the National Heart and Lung Advisory Council. (Refer to pages 22 and 23.)

- Public Law 92-423 substantially expanded the statutory mandate and responsibilities of the National Heart and Lung Institute. The President and the Congress have stated their intent to accelerate the attack on diseases of the heart, blood vessels, lungs, and blood. *So far, the resources for this accelerated attack have not been forthcoming,* and, actually, in real dollars there is less money available for heart research in 1973 than was available in 1968. The Council therefore recommends the expenditures shown in the budget in Table 1 (pages 6 and 7) as necessary for implementation of the intent of the

National Heart, Blood Vessel, Lung, and Blood Act of 1972. Specific items in the recommended budget have been discussed in detail in the April 1973 report of the Council (Appendix A). In summary, the budget reflects increases over the budget of fiscal year 1973 for support of control programs (pages 20-21 and A-20), Research Professorships (pages 11 and A-23), Professorial Research Groups (pages 11-12 and A-25), National Research and Demonstration Centers (pages 17-19 and A-30), construction (pages 19-20 and A-33), and the resumption of Research Fellowships and training grants (pages 12-16 and A-26).

- The Council also recommends additional legislation to authorize the Director of the National Heart and Lung Institute to approve grants (page 23), to change the length of the project period and the amount of the award for National Research and Demonstration Centers (page 18), and to establish an Inter-Council Advisory Committee (page 21). The Council also recommends that the present system be continued whereby the Congress establishes line items in the Federal budget for the National Heart and Lung Institute (page 21).

TABLE 1

NATIONAL HEART AND LUNG ADVISORY COUNCIL'S RECOMMENDED ANNUAL BUDGETS FOR FISCAL YEARS 1975-1979 (DOLLARS IN THOUSANDS)

Program Activities	FY 1973 (obligated)	FY 1974 (estimated)	FY 1975 (estimated)	FY 1976 (estimated)	FY 1977 (estimated)	FY 1978 (estimated)	FY 1979 (estimated)
Research Projects and Program Projects in Arteriosclerosis, Cardiac Diseases, Hypertension and Renal Diseases, Pulmonary Diseases, Thrombosis and Hemorrhagic Diseases, Sickle Cell Disease, and Multidisciplinary Studies	$109,969	$141,113	$176,400	$220,500	$231,500	$243,100	$255,300
Special Projects							
Heart Cooperative Drug Study	4,495	4,900	1,000	1,000	---	---	---
Specialized Centers of Research in Arteriosclerosis, Pulmonary Diseases, Hypertension, and Thrombosis	22,819	30,000	35,000	40,000	42,000	45,000	47,500
Control Programs[a]		5,000	14,000	30,000	31,800	33,700	35,700
Research Professorship Grants		10,000	10,600	11,300	12,000	12,700	13,600
Fellowships and Training Grants[b]	20,071	25,000	26,100	26,000	27,000	28,600	30,300
Professorial Group Grants		15,000	15,900	16,900	18,000	19,000	20,000
National Research and Demonstration Centers		24,000	24,000[c]	36,000	48,000	54,000	60,000
Construction		---	60,000[d]	30,000	30,000	0	0
Subtotal, Research Grants	157,354	255,013	363,000	411,700	440,300	436,100	462,400
Laboratory and Clinical Research	19,267	20,376	22,000	24,000	25,400	27,000	28,400
Research and Development Contracts							
Heart and Vascular Diseases:							
Myocardial Infarction	9,453	13,000	13,500	14,300	15,200	15,200	15,200
Lipid Metabolism	8,511	12,000	12,500	13,250	14,000	14,000	14,000
Hypertension Clinical Trials	5,699	8,800	9,000	9,200	9,200	9,200	9,200
Multiple-Risk Factor Trials	7,105	12,800	13,000	13,500	13,500	13,500	13,500
Education Programs (Hypertension)[a]	311	3,000	15,000	15,000	15,000	10,000	5,000
Other Clinical Applications	1,824	1,800	1,900	2,000	2,100	2,100	2,100
Subtotal, Heart and Vascular	32,903	51,400	64,900	67,250	69,000	64,000	59,000

Respiratory Diseases	3,000	6,100	8,000	10,000	10,600	11,200	11,800
Technological Applications	9,937	12,500	14,000	15,000	15,900	16,900	17,800
Blood Diseases and Resources:							
National Blood Resources	6,240	8,000	12,000	15,000	15,900	16,900	17,900
Thrombosis Clinical Trials		3,000	4,600	6,000	5,000	3,000	2,000
Sickle Cell: Research	2,232	3,700	4,000	4,500	4,800	5,100	5,400
Clinics (Health Services Administration)[a]	3,070	3,800	4,000	3,000	2,000	1,000	1,000
Subtotal, Blood Diseases and Resources	11,542	18,500	24,600	28,500	27,700	26,000	26,300
Other:							
National Plan	1,030	600	600[e]	600	600	600	600
Miscellaneous Contracts	716	892	1,000	1,000	1,000	1,000	1,000
Animal Models		1,900	5,500[f]	3,000	3,200	3,400	3,600
Subtotal, Other	1,746	3,392	7,100	4,600	4,800	5,000	5,200
Total, Research and Development Contracts	59,128	91,892	118,600	125,350	128,000	123,100	120,100
Research Management and Program Services, and Biometry and Epidemiology[g]	12,110	15,000	16,400	17,400	18,500	19,500	20,700
Grand Total	247,859	382,281	520,000	578,450	612,200	605,700	631,600
Authorization in Public Law 92-423	400,000[h]	460,000	520,000				

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[a] Under the authority of Section 414 of the Public Health Service Act as amended by the Heart, Blood Vessel, Lung, and Blood Act of 1972.

[b] Figures include all manpower programs, including Research Career and Research Career Development Awards and Pulmonary Academic Awards.

[c] The change from the previously recommended budget is related to the recommendation that the establishment of National Research and Demonstration Centers proceed at a slower rate so that performance can be monitored and problems better anticipated.

[d] The change from the previously recommended budget reflects the lack of construction funds in FY 1974; the initiation of construction would be delayed until FY 1975.

[e] The change from the previously recommended budget reflects the finding that the administration of the National Plan will probably be less expensive than originally anticipated.

[f] The increase over the previously recommended budget reflects the acute shortage of primates and the pressing need for expansion of breeding facilities, especially in relation to lung research.

[g] Costs for research management and program services are calculated as 3.8 percent of direct costs. The National Heart and Lung Institute is currently understaffed; the staff of the NHLI is one-third the size of the staff of the National Cancer Institute. Biometry and Epidemiology are included here because they relate to all divisions.

[h] Includes 25, 35, and 45 million dollars for control programs in each of years 1973, 1974, and 1975, respectively.

Recommendations for Progress in the National Heart, Blood Vessel, Lung, and Blood Program

Growth of Contract-Supported Research and Development

We often speak of biomedical research and health care as though they were quite separate. In fact, practically all of the health care that there is to "deliver" today--whatever accurate and early diagnosis, specific treatment, and prevention are available--was created by biomedical research. But the list of human diseases that we can neither prevent nor cure is still long, and it is certain that it will not get shorter without more basic and clinical research and development. The question is how best to acquire new knowledge that will in turn improve the health of our people.

The National Heart and Lung Institute, in its May 1, 1973, summary of the National Program (Reference 1), called for a wide spectrum of approaches ranging from highly structured interdisciplinary programs to individual projects initiated by independent investigators; the Institute characterized its plan as a flexible, dynamic, and continuously evolving process. When knowledge exists that can be applied at once, as in the diagnosis and drug therapy of high blood pressure, the program strategy of the National Heart and Lung Institute calls for a highly specific and structured approach with immediate and full application as its goal. But when the basic causes of disease are unknown and there is no effective means for treatment, as for atherosclerosis, the program strategy of the National Heart and Lung Institute relies on the stable support of innovative, creative, and imaginative scientists who can pursue their own best leads.

The Council agrees with that strategy; however, the Council in its report of April 1973 (Appendix A), and again in this report, gives its strongest endorsement to the current research grant program that supports basic or clinical scientists who generate their own ideas and who can pursue these ideas independently. The Council also gives its highest priority to support of research that may lead to more basic knowledge in all areas related to diseases of the heart, blood vessels, lungs, and blood and again emphasizes that increased funding for research projects *initiated by investigators* is essential to this effort.

The Council recognizes that sole dependence on investigator-initiated programs may result in neglect or under-emphasis of certain scientific areas identified as important to national needs. To prevent such neglect, the Council recommends the use of a variety of devices to stimulate fruitful work in these fields. Among these devices is the contract. Wise counsel at the national level can lead to the formulation or acceleration of some important programs when the needed research or development can be clearly predicted in orderly progression, and it can often result in the provision of valuable information difficult or impossible to obtain through the initiative of individuals.

The Council believes strongly, however, that national planning by a few highly competent individuals serving on councils, commissions, panels, committees, or task forces, should *supplement,* but not replace individual thinking by perhaps thousands of individual scientists. When the way ahead is not clear and a scientific base is lacking for a successful directed research effort, an abundance of original ideas is clearly needed; these ideas are most likely to arise unpredictably from the imagination and intuition of individual scientists and less likely to be developed centrally or by committees. There is a considerable risk for the future of the program in giving full authority for decisions about fruitful areas of scientific investigation to a relatively small group of either administrators or scientists. For these reasons, the Council recommends that

- the growth of contract-supported research and development shall not be at the expense of the support of basic or mission-oriented research initiated by individual investigators;
- long-term support of investigator-initiated grants shall be guaranteed by a line item in the budget of the National Heart and Lung Institute and at levels of approximately $141, $176, and $220 million for the years 1974, 1975, and 1976, respectively;
- the areas of research to be supported by contract and the funds allocated to each area shall be approved by the Council in advance; and
- the effectiveness of the contract mechanism--its successes and failures--shall be evaluated annually, along with the review of other mechanisms used by the National Heart and Lung Institute for the support of research, and the evaluation shall be reported to the Council.

The National Heart and Lung Advisory Council, in making these recommendations concerning the balance between research grants and contracts, is fully aware that the National Cancer Institute places much more reliance on centrally controlled decisions and allocates a larger share of its resources to contract-supported research than does the National Heart and Lung Institute. A careful, long-term study of these two philosophies of generating important new knowledge will be an important resource for the future planning of the support of science.

The growth of contract-supported research and development requires greater emphasis on the review of programs and priorities. The Council therefore reaffirms its position (page A-39) that it wishes to review, with the Director and the staff of the National Heart and Lung Institute, each of the major programs on which it advises and recommend changes in priority or emphasis that would, in the opinion of the Council, enhance progress toward the accomplishment of the goals of the National Program.

Scientists and Their Support

Recent fluctuations in Federal support of research have made careers in biomedical science far less attractive than they were some years ago and have thus been costly to a sustained research effort. The assurance of more positions with more stability will do much to attract and keep brilliant and creative scientists in heart, blood vessel, lung, and blood research. The Council strongly urges immediate activation of two new programs that would support outstanding scientists for long periods of time; it also recommends reinstitution of a program being phased out.

Research Professorships. The Council believes that a stable position should be made available in every medical school in the United States for a senior investigator who wishes to devote his main efforts to research on the heart, blood vessels, lungs, or blood. The Council envisions this mechanism as stable support, through a long-term grant and subsequent renewals, of a position for an established senior investigator who would be named by the school but who must be acceptable to the National Heart and Lung Institute. During his or her tenure in this position, the investigator would be freed from all but minor responsibilities of teaching, administration, and clinical care so that he or she could develop a vigorous program in heart, blood vessel, lung, or blood research.

- The Council therefore recommends, as a very effective means of accomplishing national goals, that the National Heart and Lung Institute establish a Research Professorship in every medical school in the United States. Approximately $10,000,000 a year should be appropriated, and allocated, for this purpose. The Council's concept of Research Professorships, their importance to the National Program, and the administrative details are presented in Appendix A (page A-23).

Professorial Research Groups. Although the recommended Research Professorship would assure support of a minimal research unit in each school for an individual research scientist, many more talented and imaginative men and women must choose and remain in careers in research related to diseases of the heart, lungs, and blood if these diseases are to be conquered. Universities, hospitals, and private research institutes do not have the financial resources to pay the salaries of these additional research scientists; their support must come from the Federal government as part of the national health effort.

- As a means of expanding the number of stable positions for creative scientists without diminishing the limited financial resources of universities and other research organizations, the Council recommends that $15,000,000 a year be allocated to the National Heart and Lung Institute for the support of Professorial Research Groups, each of which would consist of several competent investigators. At least fifty of these units should be established in this country at an average annual cost of $300,000. The Council's concept of Professorial Research Groups, their value to the National Program, and the administrative details are presented in Appendix A (page A-25).

Research Career Development Awards and Special Research Fellowships. Phasing out the current programs through which the National Heart and Lung Institute supports 200 established scientists who now devote almost full time to research important to the National Program will seriously diminish the national research effort. The Council strongly recommends that Research Career Development Awards and Special Research Fellowships be reinstituted.

Research Training

In the report of April 12, 1973 (Appendix A, page A-26), the Council stated its belief that "a critical need *now* for the long-term success of the National Program . . . is recruitment and training of young scientists. The Council sees no way to attain the long-term goal without the means to recruit talented young men and women and to provide excellent training for their research careers. These scientists-in-training . . . are absolutely essential to the Program . . . ."

The Institute, in its summary of the National Program (Reference 1, page 61) stated that the "supply of skilled manpower is an essential element in a national effort designed to advance the attack upon heart, blood vessel, lung, and blood diseases. An adequate long-range plan in an expanding program directed against these diseases will require an expanding manpower pool to conduct needed research and to replace skilled manpower lost through attrition . . . Implementation of the National Program necessitates continual assessment of available manpower--both in numbers and disciplines. The number of well-trained scientists, clinicians, and allied health professionals--in many different fields--will have to be balanced with the National Program activities. *If the needs of the Program are not met through available mechanisms, we will recommend appropriate changes* [emphasis added]. The Institute proposes to monitor the progress of the National Program with particular reference to the availability of manpower needed to achieve its objectives. As the Program moves forward, *we will develop specific recommendations as appropriate in the annual progress report* [emphasis added]."

The Council disagrees with the Institute's opinion that recommendations for developing appropriate manpower can await assessment of current proposals by the Department of Health, Education, and Welfare. Why does the Council believe that the matter is urgent? Why is recruitment and training of young scientists critical to the success of the Program? Obviously, young scientists are needed to replace present investigators who die, retire, or change careers. But the number of young scientists who must be given the opportunity to do heart and lung research is greater than the precise number to be replaced if a national goal is, as stated in the National Heart, Blood Vessel, Lung, and Blood Act of 1972, "to advance the national attack upon heart, blood vessel, lung, and blood disease." The number of young scientists enrolled in training programs must be still larger because not all who complete one or two years of training will turn out to be fully suited for a scientific career any more than all students entering law school will become distinguished lawyers. Further, in certain long-neglected areas that have now become the responsibility of the National Heart and Lung Institute, as in lung diseases, there is such a shortage of scientific personnel and scientist-teachers that a national program in research and education cannot be maximally effective until a large number of young scientists is recruited and trained. Other specific needs have been identified by recent manpower studies (Appendix B).

The phasing out of research fellowships and traineeships by the Administration has already sharply reduced research productivity because research is done not only by senior scientists but also by on-the-job research fellows and research trainees who actually conducted much of research supported by the National Heart and Lung Institute. The Council cannot believe it was the intent of the Administration to *decrease* heart research in the very same year it announced its determination to *increase* the attack against diseases of the heart, blood vessels, lungs, and blood.

This past year has been a disastrous one for training young scientists for research into the causes, prevention, and cure of diseases of the heart, lungs, and blood. In 1973, it became impossible to appoint a promising young scientist to a research traineeship or to nominate him or her for a postdoctoral fellowship. In 1973, it became impossible for a scientist to receive a Special Fellowship for the special training he or she needed to enter even a field designated by the Administration as in the national interest. In 1973, it became impossible for medical schools or research hospitals to nominate a brilliant young scientist for a five-year Research Career Development Award. In 1973, the United States became the only important Western nation that offered no federally-funded research fellowship in the medical sciences.

In 1972, there were 675 full-time and 670 part-time research fellows or trainees whose stipends were provided by the National Heart and Lung Institute. Removing on-the-job research trainees from the laboratories of our best scientists has reduced the research manpower and the productivity of many of the very best research groups supported by the National Heart and Lung Institute that were also among the best groups for research training.

The past year was particularly disastrous for the lung program of the National Heart and Lung Institute because the Division of Lung Diseases had just developed excellent training programs and was recruiting into them excellent young men and women who in a few years could fill the many vacant positions in the pulmonary divisions of most American medical schools--the very men and women who are so critically needed for research, education, and specialized clinical training in lung diseases.

The National Heart and Lung Advisory Council strongly reiterates its position that national needs in each category--teaching, research, and special types of clinical practice--must be determined at regular intervals and that sufficient funds must be made available now and in the future to support the number and variety of training programs and to provide the number of stipends necessary to meet national needs (pages A-26 and A-27).

The Council believes that the very limited resources of the American Heart Association, the American Lung Association, and other private agencies are inadequate to provide research training for medical scientists needed to implement the National Program of the National Heart and Lung Institute. The program recently announced by the Department of Health, Education, and Welfare will provide not more than $5,500,000 the first year for support of *all* research fellows in the heart, blood vessel, lung, and blood fields. The Council reminds the Congress that stipends in 1972 to research fellows and trainees of the National Heart and Lung Insitute alone would have required $18,000,000 (at the proposed new rate), which would not have allowed for program expansion. Thus, the new training program of the Department of Health, Education, and Welfare cannot possibly meet the needs of biomedical science; it is a contraction of the training effort, not an expansion.

The Council believes that the responsibility for training young medical scientists is clearly that of the Federal government and not that of state or local governments. Young scientists are a valuable national resource and their training is a national obligation because their work benefits all of our people in all fifty states. No one would ever consider the possibility that each state and each community should make its own medical discoveries and reserve them for its own residents. Moreover, available resources for the support of medical research and training vary greatly among the states and regions. National support is needed to prevent local inequities related to economic, geographic, ethnic, or other factors. Unlike physicians who usually practice in the state where they have received their medical or postgraduate education, medical scientists who are trained in a limited number of centers of excellence more often spend their research and teaching careers in other medical schools, hospitals, and institutions in other states.

The Council believes that the National Heart and Lung Institute should utilize two mechanisms of support for training: (i) fellowships that will support individuals who would benefit most by intensive research with a distinguished mentor in a special area, and (ii) training programs in highly qualified departments that will support individuals who require broad interdisciplinary research training, such as young physicians, engineers, physicists, and mathematicians who wish to enter into a research career in the biomedical sciences.

Whatever the mechanism, no more than two months should elapse between receipt of a completed application and the decision as to whether the fellowship or traineeship would be awarded; medical science may be losing highly qualified young men and women because of the uncertainties associated with the previous nine-month process of review and announcement of award.

The Council recommends that $26,100,000 be allocated for training in cardiovascular, pulmonary, and blood diseases in fiscal year 1975.

The Council realizes that these recommendations run counter to those of the Department of Health, Education, and Welfare and of the Office of Management and Budget. The President and the Secretary of Health, Education, and Welfare, however, have appointed four groups that have advised on health policy in this area--the President's Science Advisory Committee, the National Heart and Lung Advisory Council, the National Cancer Advisory Board, and the President's Advisory Panel on Heart Disease--and all four have stressed the importance of maintaining strong graduate training programs for biomedical research. Further, the President in public statements and the Congress in enacting the National Heart, Blood Vessel, Lung, and Blood Act of 1972 have also stressed the need for training. All of these statements on training for biomedical research are quoted or referenced below.

- PANEL ON BIOLOGICAL AND MEDICAL SCIENCE OF THE PRESIDENT'S SCIENCE ADVISORY COMMITTEE, 1972, "Scientific and Educational Basis for Improving Health" (Appendix C).

- PRESIDENT'S ADVISORY PANEL ON HEART DISEASE, 1972. Note: The Panel's report, submitted to the President in September 1972, has not yet been released to this Council, to the Congress, or to the public. We understand that the report contains a strong recommendation for continuing research training programs and fellowships. Perhaps the Congress can obtain a copy of the report for verification.

- NATIONAL HEART AND LUNG ADVISORY COUNCIL. *National Heart, Blood Vessel, Lung, and Blood Program. Volume II: Report of the National Heart and Lung Advisory Council*, April 12, 1973 (Appendix A, page A-26).

- NATIONAL CANCER ADVISORY BOARD, January 1973. "At the junior level, a continuing influx of able young scientists is of overriding importance. It is these young people who can meet the vast problems of cancer with few fixed attitudes and preconceptions, yet at the height of their intellectual and physical powers. It is they who are especially likely to formulate new questions and find new answers toward overcoming cancer. *Continuation and expansion of existing training programs are essential to ensure that these young scientists are attracted and adequately prepared to join in the National Cancer Program."*

- NATIONAL HEART, BLOOD VESSEL, LUNG, AND BLOOD ACT OF 1972: Section 413(a)(7) and Section 415(a)(1) and (2) [Reference 1, pages 65 and 67].

- THE PRESIDENT OF THE UNITED STATES: "Scientific activity cannot be turned on and off like a faucet. The withdrawal of support disperses highly trained research teams, closes vital facilities, loses spinoff benefits, and disrupts development momentum. The current Johnson Administration has even struck at the lifeline of our future progress--science education . . . Especially hard hit in the reductions is aid for postdoctoral students who serve as graduate student instructors. The decline of science education is the most damaging indictment of present Administration policy; it threatens to cripple the national effort in science for years to come." --Richard M. Nixon, October 1968, as quoted in *Science* 182:265, 1973.

It is the opinion of the Council that the Congress should try to resolve the present conflict between the Administration and the highly qualified consultants that the Administration has appointed as its own advisers.

Peer Review

As stated earlier, the Council gives its highest priority to the support of investigator-initiated research. Indeed, the success of the biomedical research effort in the United States has come about in important measure because the most promising research has been selected for support from public funds. But not all projects proposed can be supported by Federal funds and some are not worthy of support. Decisions about which projects to support and in what order of priority require the mature and objective judgment of many scientists based on their up-to-date knowledge in many specialized areas, their long and intimate experience with a variety of techniques and with the appropriateness of methods and other resources, their evaluation of the background and productivity of the investigator, and their estimate of the likelihood that the proposed research would contribute new knowledge not already available.

Under the authority of Public Law 92-423, the Director of the National Heart and Lung Institute may approve grants for research and training in heart, blood vessel, lung, and blood diseases "after appropriate review for scientific merit and recommendation for approval by the Council." To fulfill this statutory requirement, the National Heart and Lung Advisory Council requires the highest quality of initial review for scientific merit of grant applications by the study sections and other initial-review groups that provide the first review in the dual peer-review system utilized by the National Institutes of Health. The Council believes that the present system of initial peer review by standing committees of leading scientists in appropriate disciplines constitutes the most effective system that has been devised for purely objective technical and scientific review. The system of peer review developed and utilized by the National Institutes of Health is recognized worldwide as one of the most successful accomplishments of the United States' public support of science. This system of peer review has assured high quality and outstanding productivity in the total research effort. Yet, criticisms of this review system by the Office of Management and Budget have overlooked the absolute requirement for quality.

The Office of Management and Budget has criticized the peer-review system used by the National Institutes of Health as supposedly more expensive than "in-house" review. But elementary calculations reveal that (i) the amount of money expended for scientific and technical review is small compared to the amount of funds awarded (less than one percent), (ii) there are simply not enough scientists on the staff of the National Heart and Lung Institute to critically assess even a small fraction of research proposals in the many different fields, and (iii) the errors in scientific judgment that would result from central review by administrators no longer actively engaged in research would make "in-house" review costly to the nation because research of poor quality is not only noncontributory, it is wasteful and counterproductive since poor experiments must be repeated and corrected.

The Office of Management and Budget has also urged that more administrative control be exercised over the current system of peer review. For the reasons listed above, too much interference in the guise of "administrative control" could seriously weaken the system by the introduction of criteria for allocation of grant funds based on factors other than merit and quality.

The study section mechanism of peer review has also been criticized as not being objective because judgments are made by the nation's scientific community who are not disinterested individuals. To eliminate this criticism, we would end with a situation in which the members of the review groups would know little or nothing about the problems, and the judgments of these groups would be of no value to the National Heart and Lung Advisory Council.

- The Council urges that any changes in the procedures used by the National Institutes of Health for the merit review of grant proposals be made only with full recognition of the necessity for the highest quality of review for scientific and technical merit. No changes in the current procedures should be permitted until a carefully designed and well controlled trial of a new method has been applied to part of the programs of the National Institutes of Health (under conditions that would allow critical comparative evaluation) and the new method has been clearly proved to be superior to the present system of peer review.

The Council also wishes to reaffirm its position regarding the peer review of proposals for centers and contracts (page A-29). The Council believes that the system of peer review used by the National Institutes of Health has been as effective for program project grants and specialized centers of research as for individual projects. The Council believes that the same exacting review must be utilized for the evaluation of proposals for the new National Research and Demonstration Centers and for contracts.

- The Council strongly advises that the system of peer review used by the National Institutes of Health to evaluate research grant applications be applied in similar form to all programs of the National Heart and Lung Institute.

National Research and Demonstration Centers

Section 415 of the National Heart, Blood Vessel, Lung, and Blood Act of 1972 (Reference 1, page 67) authorizes the Director of the National Heart and Lung Institute to establish centers for basic and clinical research into, training in, and demonstration of, advanced diagnostic, prevention, and treatment methods, including methods of providing emergency medical services, in heart, blood vessel, lung, and blood diseases. The Act authorizes as many as fifteen such centers for heart, blood vessel, and blood diseases and fifteen for lung diseases. The Council endorses the concept of and need for such centers that include the important components of education and demonstration in addition to basic and clinical research and believes that these centers will be able to promote the effective and rapid translation of research advances into the realities of health care. The Council approves the program announcement, guidelines, and schedule for review of applications and their funding that were distributed by the National Heart and Lung Institute in August 1973 (Appendix D).

The process for the final selection of recipients of these center grants will be extraordinarily important, since the final selection will largely determine the type or types of centers that will evolve under this legislation. The Council therefore wishes to participate actively in selecting from the meritorious proposals the recipients of grants for National Research and Demonstration Centers.

The Council recommends that the National Heart, Blood Vessel, Lung, and Blood Act of 1972 be clarified or revised as follows.

- The Council recommends, for two reasons, that Section 415 of the Act be modified to permit a seven-year period of support for a National Research and Demonstration Center, rather than the specified five years: (i) the complexity of a center necessitates a major commitment of staff and facilities, development of new relationships with the community, and probably construction of new laboratories, and (ii) the Council believes that stable support of scientists is conducive to increased productivity.

- The Council also recommends that the upper limit for the annual budget of such a center refer only to direct costs and that realistic allowances be made when increased costs of living bring the budget above the present $5,000,000 ceiling. The Council therefore recommends that the last paragraph of Section 415 of Public Law 92-423, be amended to read: the aggregate of payments (other than payments for construction made to any center under such an agreement) may not exceed $5,000,000 *direct costs* in any year. (Adjustments for increased costs of living shall be allowed when the annual budget is at the $5,000,000 ceiling.) Support of a center under this subsection may be for a period of up to seven years and may be extended by the Director of the Institute for additional periods of not more than seven years each, after review of the operations of such center by an appropriate scientific review group established by the Director.

- The Council recommends that only four to six such centers be funded now and that sufficient time be permitted for careful review and evaluation of the strengths and weaknesses of the program before funds for the full number of authorized centers are requested. The Council therefore asks that $24,000,000 be allocated for those centers in fiscal years 1974 and in 1975 and that the allocation be increased to $60,000,000 by fiscal year 1979. The Council asks that Congress appropriate funds as a line item specifically to initiate this program and that these be *in addition to* appropriations for other research programs.

- Although the Council recognizes the importance of paying the costs of constructing parts of these centers, it believes strongly that funds appropriated by the Congress for construction should be available where they will do the most good for the overall program of the National Heart and Lung Institute, whether construction is for a center or for other needed facilities.

Developing Research, Training, and Demonstration in Institutions with Little or No Participation in Programs of the National Heart and Lung Institute

In addition to establishing National Research and Demonstration Centers, the Council believes that there is a need for developing research in institutions that now participate only to a limited extent in programs of the National Institutes of Health. The Council believes that the research interests of all of the National Institutes of Health will be best served in the long run if more research of quality comes from more of the nation's medical schools and if, in addition, scientists in a variety of settings, including independent research institutes, industry, colleges, and universities, are engaged in health-related research and development. The Council is developing a proposal which it hopes will broaden and strengthen the base of the national research effort in heart, lung, and blood diseases.

Since all of our national health goals would be enhanced by the participation of more scientists in a greater variety of settings, the Council recommends that the National Institutes of Health initiate a study of means for encouraging quality research in institutions that at present do not participate, or participate only to a limited extent, in biomedical research programs related to the missions of the National Institutes of Health.

Construction of Facilities for Biomedical Research

The Council places a very high priority on the construction of research facilities. The previous report of the Council (Appendix A) and the National Heart, Blood Vessel, Lung, and Blood Act of 1972 (Reference 1) both call for National Research and Demonstration Centers; in addition, the Council's report calls for support of more than a hundred Research Professorships and fifty Professorial Research Groups and for an expansion of research supported by grants and contracts. All of these activities will require additional research laboratories. The success of the National Program depends upon more, and more modern, research facilities.

Both the National Heart and Lung Institute's Summary of the National Program (Reference 1, pages 58 and 60) and the Council's previous report (Appendix A, pages A-33 and A-36) call for funds for the construction of new research facilities and the modernization of existing facilities. The Institute asked that $70,000,000 be appropriated over a three-year period; the Council specified $120,000,000 for the three-year period. This money should be appropriated in a line item as new funds.

- Because the results of research benefit the entire nation, the Council urges that recipient institutions not be required to provide matching funds. National interests are best served by making construction funds available to those scientists and institutions that, given additional facilities, can make the greatest contribution to the National Program rather than to those whose scientific contribution may be less but who have access to non-Federal funds with which to match Federal funds.

The availability of complete Federal funding for construction would permit financially troubled schools to apply and so increase the total research effort toward achievement of national goals, which would, in turn, lessen the redistribution of scientists from poor to more affluent schools.

- The Council asks that funds for construction not be limited to National Research and Demonstration Centers but granted for the construction or modernization of any facilities essential to the success of the National Program.

If the Congress wishes to be consistent in its goals to conquer cancer and heart diseases, the Congress must supply new facilities for research on diseases of the heart, blood vessels, lungs, and blood. The Council notes that an essential component of the plan of the National Cancer Advisory Board is funds for construction of new physical resources; the National Cancer Institute received an allocation of $49,000,000 in the President's budget for 1973 and an additional $20,000,000 in the budget for 1974. There has been no lack of worthy requests for these funds.

Education, Control, and Prevention

It is through implementation of the disease prevention, control, and education programs that the most immediate transfer of research knowledge to the practical public good can be accomplished. Demonstration projects noted in the previous report of the Council should be developed (Appendix A, pages A-19 and A-20). Ideally suited for immediate implementation are six programs: (i) screening of populations for blood-lipid levels to determine susceptibility to atherosclerosis, (ii) education of the public and physicians in the importance of case-finding in hypertension, appropriate treatment of hypertensive patients, and maintenance of treatment, (iii) early diagnosis of congenital heart lesions and use of corrective or palliative surgical procedures to save the lives of those with these disorders, (iv) prenatal detection of respiratory distress syndrome and assignment of the mother and unborn baby to emergency care units in regional centers where intensive care, including continuous positive-airway-pressure, can save lives, (v) establishment of a national blood bank system, and (vi) education of the public regarding early warning signs of heart attack and stroke.

Increased emphasis is needed on physician education and on research into motivation of the public to seek, accept, and continue therapy, including the cessation of smoking.

The National Institutes of Health

The ability of the National Heart and Lung Institute to accomplish the goals of the National Program is dependent, in large part, upon the policies and operational procedures of the parent organization of which the Institute is only one component. Legislation should therefore be considered for certain operational aspects of the National Institutes of Health that affect the functioning of the National Heart and Lung Institute.

Congressional Determination of the Budget of the National Heart and Lung Institute. The Council believes that the programs of the National Heart and Lung Institute are so important to the welfare of the American people that the major decisions concerning these programs should be in the public arena. Specifically, the Council recommends that the present system by which the Congress now establishes separate line items in the Federal budget for the National Heart and Lung Institute be continued to assure public and congressional access to both planning and review of the programs of the Institute.

Inter-Council Advisory Committee.

- The Council recommends that an Inter-Council Advisory Committee composed of two scientists from each National Advisory Council of the National Institutes of Health and appointed by each Council be established through legislation.

The Inter-Council Advisory Committee would assure direct communication, where none now exists, among the National Advisory Councils of the National Institutes of Health and between the Councils and the Director of the National Institutes of Health. The Committee would function in an advisory capacity to the Director of the National Institutes of Health and meet at least three times each year.

Appointment of Director of the National Institutes of Health. The National Institutes of Health has been relatively free of direct political control, and it should remain so. Legislation should be considered that would preserve this freedom to operate strictly within the framework of national health goals and establish qualifications of the Director of the National Institutes of Health, including scientific, administrative, and leadership criteria. Criteria for the position of Director of the National Institutes of Health and procedures for the selection of the individual to fill this position should be established by law. For example, the National Science Foundation Act of 1950 (Public Law 507, as amended by Public Law 92-484) specifies that the Director of the Foundation "shall be appointed by the President by and with the advice and consent of the Senate. Before any person is appointed as Director, the President shall afford the [National Science] Board an opportunity to make recommendations to him with respect to such appointment."

- The Council recommends that legislation be enacted that would make the appointment of the Director of the National Institutes of Health by the President subject to the advice and consent of the Senate and that would assure an Inter-Council Advisory Committee of the opportunity to make recommendations to the President with respect to such appointment.

Appointment of Director of the National Heart and Lung Institute.

- The Council recommends that the Director of the National Heart and Lung Institute, as well as of each institute within the National Institutes of Health, be appointed by the Director of the National Institutes of Health after full consultation with an Inter-Council Advisory Committee.

- Accomplishment of the goals of the National Program requires outstanding scientific leadership. To retain the present Director and his staff and to attract the necessary additional full-time, senior-level personnel to the National Heart and Lung Institute, the Federal government should provide a salary structure that would permit the Institute to compete for the best scientific minds.

Appointment of Council Members. Chapter 9-25 of the *General Administration Manual of the Department of Health, Education, and Welfare* states that in the appointment of members of public advisory committees, the Secretary of the Department shall give consideration to professional qualifications, geographic representation, and representation of all possible viewpoints including those based on sex, age, race, cultural, and socioeconomic backgrounds. The policy that governs appointment of members of public advisory committees also requires that the nominating official carefully examine the nominee's *curriculum vitae* and his competence and suitability for government service, and the member's performance, once he or she is appointed, be evaluated periodically to determine whether he or she shall be retained on the committee. Nevertheless, recent experience of the National Heart and Lung Advisory Council has shown that individuals can be appointed to the Council--the National Heart and Lung Institute's highest advisory body--who have neither the qualifications, interest, nor intent to serve as Council members. Such inappropriate appointments reduce the number of working Council members and diminish the status, and hence, the effectiveness of the advisory body.

The Council recommends that of the eighteen members appointed by the Secretary, thirteen be selected from among the leading medical or scientific authorities who are skilled in the sciences related to diseases of the heart, blood vessels, lungs, and blood and five be selected from the lay public. These lay members should be chosen for interest in the mission of the National Heart and Lung Institute and for special competence that can be brought to the deliberations of the Council. The special competence might be in areas such as public affairs, community needs, economics, education, management, communications, or the social or physical sciences.

- The Council also recommends that legislation be enacted that would establish minimal qualifications for appointment to the National Heart and Lung Advisory Council. The Council has categorized its activities to meet its increased and broader responsibilities, and this type of organization by activities requires that the qualifications for lay members include a demonstrated interest in the health of the nation's people and especially in disorders of the heart, blood vessels, lungs, and blood; for scientific members, a demonstrated competence in biomedical research and training and (or) in clinical practice; and, for all members, a written commitment, before appointment becomes final, to participate fully in all of the activities of the Council, including expression of the member's point of view either orally or in writing. A mechanism should be included for replacing a Council member whose performance does not meet the basic requirements for this position.

Authority of the Director to Approve Grants. The National Heart, Blood Vessel, Lung, and Blood Act of 1972 (Public Law 92-423) provides that the Director of the Institute may approve grants for research and training "in amounts not to exceed $35,000 after appropriate review for scientific merit but without review and recommendation by the Council." The implementation of this provision will require clarification of the direct costs intended.

- The Council recommends that the wording of Section 5 of Public Law 92-423, as related to the amendment of Section 419A(c)(1) of the Public Health Service Act, as so redesignated by Section 3 of Public Law 92-423, be amended to read: in amounts not to exceed $35,000 *direct costs* after appropriate review for scientific merit and according to guidelines established by the Council, but without review and recommendation by the Council.

- The Council also recommends that the provision for awarding grants that do not exceed $35,000 direct costs without review and recommendation by the Council be extended to encompass the grant programs of all of the awarding components of the National Institutes of Health so that inequities in the time required for obtaining grants may be removed for the benefit of all grantees of the National Institutes of Health.

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Appendix A

National Heart, Blood Vessel, Lung and Blood Program, Volume II: Report of the National Heart and Lung Advisory Council, April 12, 1973

Appendix A

National Heart, Blood Vessel, Lung and Blood Program, Volume II: Report of the National Heart and Lung Advisory Council, April 12, 1973

I. INTRODUCTION

The National Heart, Blood Vessel, Lung and Blood Act of 1972 specifically states that the Director of the Institute, with the advice of the National Heart and Lung Advisory Council, shall develop a plan for a National Heart, Blood Vessel, Lung and Blood Disease Program. This report is the advice of the Council for such a program to advance the attack against these diseases and improve the management of the nation's blood resources.

The maturation of many research-proven ideas, methods and technologies, viewed in relation to the increasing health problems of heart, blood vessel, lung and blood diseases, convinces the Council that the next few years could bring significant new discoveries and health benefits for the American people. Great strides have been made in prevention, both real and potential, in diagnosis and in medical and surgical treatment of these major diseases. The result has been new hope for patients suffering from them. In fact, death rates from some of these diseases have levelled off or even decreased in the last few years.

The public deserves the fullest application now of the preventive, diagnostic and treatment measures already developed through research. At the same time, the research and clinical momentum generated in the unparalleled period of expansion of scientific medicine in the past two decades must be sustained, for it is through this momentum that important new knowledge will be generated and then translated into health benefits for all.

At the present time, the diseases addressed by the National Program together cause more than one million deaths each year in the United States. In their chronic forms, they affect more than 30 million Americans. The loss of productivity through disability alone is enormous.

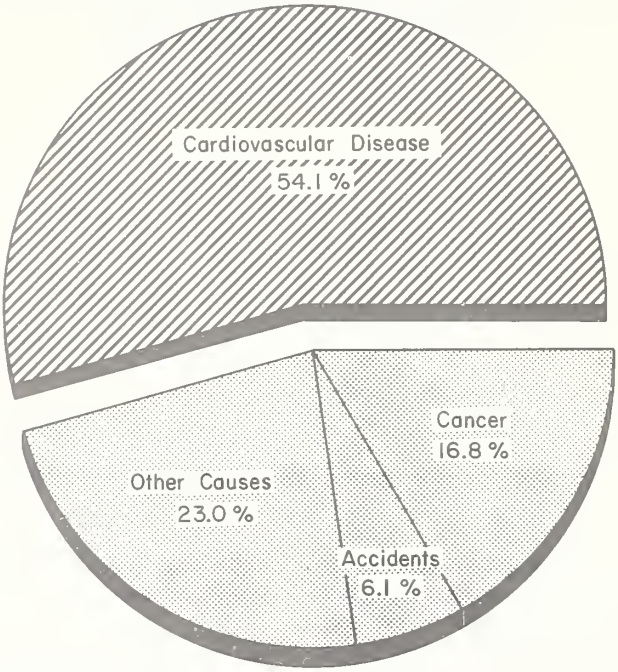
Diseases of the heart and blood vessels are by far the largest problem. They account for more than half of the annual deaths from all causes in the United States (Figure 1), thus making this country's rate among the highest of the developed nations. Although the toll is heaviest in the older ages, a quarter of the deaths occur under age 65.

- Coronary heart disease, which includes heart attack, causes 675,000 deaths each year, many of which occur suddenly and unexpectedly; four million persons in this country have had a heart attack or suffer from angina pectoris.

- Every year 200,000 individuals die as the result of a stroke; 1.7 million persons are at least partially incapacitated from having suffered a stroke.

Figure 1

DEATHS FROM ALL CAUSES, UNITED STATES, 1967



- Hypertension, which predisposes to stroke and heart failure, affects 23 million Americans, 13 million under age 65.

If heart and blood vessel diseases could be eliminated as causes of death, the gain in life expectancy would approach 11 years, more than four times the gain that would be achieved by the elimination of any other cause of death.

The chronic lung diseases are also a serious health problem.

- Emphysema, chronic bronchitis and asthma afflict 14 million individuals, more than 11 million of them younger than age 65.

- Each year, emphysema, pneumonia and hyaline membrane disease kill 100,000 Americans.

Thrombosis and diseases of the blood are responsible for much acute and chronic disease.

- Venous thrombosis and pulmonary embolism strike 300,000 persons annually.

- Sickle cell anemia and hemophilia afflict 50,000 to 75,000 persons.

The impact of the heart, blood vessel, lung and blood diseases on the nation's economy is great. Each year, health expenditures for these diseases are more than $9 billion, and the value of present and potential earnings lost because of the illness and death they cause amounts to at least an additional $29 billion.

The Council believes that a plan for a National Program for the next five years will serve the following purposes:

- Provide a basis for decisions concerning appropriate support for needed efforts in the heart and blood vessel, lung and blood areas;

- Ensure proper priority and sequence of implementation;

- Provide a basis for determining scientific manpower needs for research to sustain the total program;

- Facilitate coordination of the efforts of all Federal agencies in the heart and blood vessel, lung and blood fields;

- Make it possible to delineate Federal responsibilities so that state, local and private sectors can plan their participation and responsibilities accordingly;

- Enable orderly and systematic review and analysis of progress of the Program.

The Council believes that a National Program centered in the National Heart and Lung Institute is more appropriate than a variety of local programs. It should make possible a coordinated rather than an uncoordinated, fragmented effort, and should help to assure cooperation, communication and interchange of ideas and results among the many agencies, institutions and scientists involved in the total effort.

Within the framework of a National Program, priorities can be set and progress measured effectively. An analysis of progress undoubtedly will suggest modifications in the Program. A degree of flexibility must be maintained to accommodate changes.

The Council's report deals with the generation of new knowledge; the development of new diagnostic, treatment and prevention techniques and their evaluation; and the demonstration of their applicability. Although the Council addressed itself to matters of patient care and widespread application of diagnostic and treatment programs, it believes these matters can best be handled by other sectors of the private and public health care establishment. However, the Council recognizes that the National Heart and Lung Institute must interact regularly and systematically with other agencies responsible for health care in order to assure the most timely and effective application of the results of its work.

The Council believes that much attention must be devoted to developing the nation's health resources. One example is an urgent need for a blood bank program to husband this vital resource. The Council believes that scientific knowledge is also a major national resource and, more importantly, one which should be immediately available to people in all the states of the nation. An adequate system for dissemination of information could accomplish this purpose. The development of these and other national resources to benefit the health needs of the nation presents a real opportunity and challenge.

II. GOALS

The immediate goal is to secure the additional knowledge and techniques needed for early diagnosis and effective treatment of existing disorders of the heart, blood vessels, lungs and blood and to demonstrate their application to the health care problems of the country. The long-range goal is prevention and elimination of disease. Before presenting specific high-priority programs, the Council believes it is important to state clearly the lessons we have learned about scientific discoveries necessary to solve the great problems of these diseases.

First, although we have learned much about the heart and blood vessels, lungs and blood, our areas of ignorance are still far greater than areas of complete understanding. The following are but a few examples:

- In the past three decades, we have learned how to prevent rheumatic fever and rheumatic heart disease by treating the antecedent streptococcal infection with penicillin. For those patients who developed rheumatic heart disease before that time, we have learned how to repair or replace badly damaged heart valves. But we still do not know how to ensure that every child with a sore throat has a throat culture or how to treat all susceptible children long enough to prevent heart disease.

- In the past three decades, we have learned how to use new drugs to lower blood pressure in hypertensive patients to lessen the risk of strokes and heart failure. But we still do not know what causes most forms of high blood pressure, how to motivate the population to be screened for high blood pressure, or how to initiate and maintain effective therapy in all those with high blood pressure.

- We have learned how to catheterize the hearts of small babies to identify congenital heart lesions, and how to correct them by open heart operations. But we do not know how many congenital cardiac defects are genetic or how many reflect the environment of the fetus, and, except for some defects known to be due to rubella virus, we do not know how to prevent congenital heart disease.

- We know how, by surgical procedures, to correct or by-pass atherosclerotic obstructions in the arteries. But we do not know how to prevent atherosclerosis or how to diagnose and treat it early.

- We have sophisticated physiological tests that tell us precisely the functional defects of diseased lungs. But we do not know the cause of pulmonary emphysema, how to stop its progress even if detected early, or how to prevent heart disease caused by emphysema.

- We know the specific clotting factor whose deficiency causes hemorrhage in patients with hemophilia. But to treat these patients requires harvesting the factors from more than 50 percent of the national blood supply. We do not know how to obtain these factors with reasonable cost-effectiveness; neither have we discovered alternative treatments.

We tend to obscure our ignorance by making it seem that a problem has been solved when it has, in fact, been only half solved. We must face up to our ignorance in many matters and recognize that an entirely different type of knowledge than we now have will be necessary to fully solve these problems.

Second, by far the surest way to save the public's health dollar in the long run is to obtain a clear enough understanding of the mechanisms causing heart, blood vessel, lung or blood diseases to permit prevention or complete cure. The less we know about a disease, the less specific is the treatment and the greater the cost. Specific prevention and definitive treatment usually cost relatively little and are easily translated into effective action.

- Twenty-five years ago, all we could offer patients with tuberculosis was nonspecific sanatorium or surgical care which was very costly and not very effective. We now have specific chemotherapy; it is both effective and cheap.

- Finding factors that produce rheumatic fever and a way to prevent rheumatic heart disease have proved to be far less costly than modern diagnosis and surgical treatment of patients with damaged heart valves.

- It is far less expensive to provide rubella vaccine to future mothers before their child-bearing age than to perform heart surgery to correct the congenital heart defects that rubella causes.

In the long run, investment in fundamental and clinical research to learn the mechanisms and causes of diseases and to prevent them has been far less expensive than paying for half-way measures, the results of which can only be a reduction in disability.

Third, to bring the best possible health care to the people of our country and, ultimately, to prevent disease, we must accelerate two campaigns: (1) to apply what we now know as effectively as we can, and (2) to gain new knowledge and new understanding—of the basic biological processes and mechanisms underlying normal heart, blood vessel, lung and blood functions; of the biochemical, genetic, nutritional, behavioral, social, environmental and other processes that lead to diseases of these systems; and of ways to prevent or counteract these diseases.

Both campaigns are essential. We cannot tell patients who are ill with a disease that we are concerned only with the prevention of such disasters in others; for them, having the best available treatment may be a matter of life or death. We must not have all basic research and no applied; but neither must we have all applied research and no basic. Neither should these campaigns be sequential. We cannot double applied research and stop basic research for five years and then double basic research and stop applied research for five years.

Fourth, contrary to popular conception, it can be documented that important new knowledge rarely comes through sudden "breakthroughs"; research goals are almost invariably reached by a steady accumulation of knowledge—bit by bit—until finally the last bit secures a major advance. In biological research, crash programs often crash!

Similarly, great clinical advances rarely burst upon the scene as the result of mission-oriented, commission-directed programs, but come at a logical time when a broad advance in basic biologic science (often not directed toward the prevention or treatment of a particular disease) has made the clinical discovery nearly inevitable. Mission-oriented programs can then accelerate the achievement of the final specific goal.

One of the most important and certainly the most dramatic advances of the past two decades has been the development of open heart surgery. To the lay public and to many physicians and scientists, open heart surgery stands out as a great achievement of mission-oriented, goal-directed research. And it is true that the development (by mission-oriented research) of a pump-oxygenator was absolutely essential to open heart surgery. But it is crucial to the understanding of scientific discovery to realize that the development of a pump-oxygenator was itself possible only because of many earlier discoveries that were not mission-oriented, such as:

- Discovery by a physiologist of heparin, a substance that prevents blood clotting;

- Discovery by an immunologist of blood groups that led to blood typing and safe blood transfusions (and today to safe blood use in pump-oxygenators);

- Studies of red blood cells, their natural lifespan and how to preserve their life outside the body—which led to the storage of blood for emergencies and then to blood banks;

- Studies by biochemists on the diffusion and exchange of oxygen and carbon dioxide, essential for construction of artificial oxygenators.

But successful open heart surgery required more than a pump-oxygenator. It also required accumulation of considerable knowledge in many biologic fields. It had to await basic research on the heart's conducting system and on arrhythmias that led to devices to control serious arrhythmias; on fluid and electrolyte metabolism that permitted long surgical procedures; and on anesthesia, respiratory physiology and mechanics of ventilation that permitted proper ventilation and anesthesia of a patient with an open chest. Other important contributions were the discovery of the electrocardiograph, of hypothermia, of techniques for electively stopping and restarting the heart, and of chemotherapy and antibiotics.

Knowledge flows in both directions. Thus, the identification and study by surgeons of new problems in patients who have undergone open heart surgery stimulated renewed research efforts and produced new knowledge in basic research in many fields.

A recent analysis of 175 scientific discoveries that had to be made to permit the great clinical advances of the 1950's and 1960's in the treatment of heart, blood vessel, lung and blood diseases, showed that 36 percent were basic discoveries completely unrelated to these diseases; 31 percent were made in basic research designed to contribute to solution of a clinical problem; and 33 percent were made as a result of applied mission-oriented research. Therefore, an essential part of the Council's philosophy is that both applied science (and development and engineering) and basic science are essential. The Council hopes that the public will come to recognize that the *last event* leading to a dramatic clinical advance is possible only because of scores or hundreds of earlier discoveries. We should not talk in terms of supporting either basic *or* applied, or targeted *or* nontargeted research. We must support mission-oriented research to alleviate suffering and reduce disability and we must support nontargeted research to uncover knowledge not yet imagined by the most competent commissions, panels or task forces appointed by public or private agencies.

Fifth, the all important clue to the cause and prevention of atherosclerosis or emphysema, as well as many other diseases, may come from scientists working in an unrelated field.

- When Karl Landsteiner discovered human blood groups, he was investigating basic problems in immunology; he was not then aware he was making safe blood transfusion possible.

- When Roentgen discovered X-rays, he did not realize it would enable physicians to visualize the heart, lungs, and blood vessels of their patients.

- When Cournand and Richards passed a catheter into the heart of a man, it was not to develop methods of diagnosing congenital or acquired heart disease; they wanted to measure the oxygen in mixed venous blood to learn more about basic physiologic problems of pulmonary gas exchange.

- When Alexis Carrel developed the new science of suturing blood vessels and transplanting arteries, veins and whole organs, it was a necessary first step to his main goal of studying basic life processes and the metabolic requirements of each organ for optimal function.

- When Davies and Brink devised an "electrode" to measure the oxygen used by nerve cells, they had no idea that it would become an essential monitoring device in every intensive care unit for measuring blood oxygen.

These examples make it clear that a successful effort against heart, blood vessel, lung and blood diseases will depend, in part, upon strong and sustained support of basic and mission-oriented research in other fields of science, as well as those fields directly concerned with these diseases.

III. PREVENTION, DIAGNOSIS AND MANAGEMENT OF SPECIFIC DISEASES: RECOMMENDATIONS

Late in 1972, a Committee consisting of four Panels—one each for heart and blood vessel, lung, and blood diseases and a separate one for blood resources—was established to assist in the formulation of a coordinated plan for a National Heart, Blood Vessel, Lung, and Blood Program. These consultant Panels, with the help of approximately 250 additional medical and scientific advisors, assessed present knowledge and identified areas in which progress against heart, blood vessel, lung and blood diseases may be expected or is urgently required. The following four sections are the Council's evaluation of the four separate Panel Reports and the summation by the Panel Chairmen.

As indicated in each Panel Report, there are many urgent problems in each disease area. The Council believes that proper application of existing knowledge now would decrease illness and death from heart and blood vessel, lung and blood diseases. At the same time, however, there is need for new knowledge and for the entry of this new knowledge into the management of disease. A nationwide, coordinated effort to exploit our present understanding, to remedy current inadequacies, to seek new knowledge, to develop new techniques, and to establish new directions of inquiry seems particularly timely.

1. HEART AND BLOOD VESSEL DISEASES

Heart and blood vessel diseases have been the major cause of death in the United States since the 1920's. Although there has been a decline in death and disability attributable to rheumatic fever, hypertension and stroke, the overall rate for all heart and blood vessel diseases is still 54 percent of all deaths in the United States.

- Atherosclerosis, including coronary heart disease and stroke, accounts for more than 800,000 deaths each year.

- Hypertension, although not a common direct cause of death, affects about 10 percent of the total population of this country and about 30 percent of the black population.

The Council concurs with the conclusion of the Heart and Blood Vessel Diseases Panel that, in the long run, the most rewarding approach will be the development of more effective methods for the prevention of heart and blood vessel diseases based upon a better understanding of the mechanisms of specific disease entities.

Atherosclerosis

Atherosclerosis is a slowly progressive, long-term disease that probably starts in childhood. It may produce no symptoms and, therefore, go undetected for years but eventually may result in a heart attack or stroke. Although many factors—such as elevated blood lipids, hypertension, and cigarette smoking—probably contribute, how atherosclerosis develops is not understood. Further, studies of its natural progression are sharply limited in effectiveness because there is no simple way of detecting it until the arteries become so narrowed that painful symptoms result from the decreased blood supply, or until the formation of a blood clot (thrombosis) suddenly occludes an artery causing a heart attack or stroke.

The Council gives highest priority to understanding the basic mechanisms of atherosclerosis through studies of the cellular biology of the blood vessel wall and its interaction with circulating blood and its components.

The Council also emphasizes the need for development of simple, noninvasive techniques for detection of asymptomatic atherosclerosis.

Intervention trials, such as modifying diet, stopping smoking, controlling hypertension, and improving physical fitness, now must go on for many years because they must use as end points the occurrence of such events as heart attacks and strokes. Faster, more economical, and more definitive clinical trials would be possible if simple methods for detection were available.

Clinical intervention trials need to be conducted, and because current end points are crude, they will require large numbers of subjects studied over long periods if meaningful results are to be obtained.

Thrombosis

Thrombosis—the formation of a clot in a blood vessel—is intimately related to atherosclerosis. It not only contributes to the progression of the atherosclerotic lesion but also is responsible for many of the clinical complications of atherosclerosis. It may occur suddenly on an atherosclerotic plaque, causing severe or total occlusion of a blood vessel to the heart or brain, thus resulting in a heart attack or stroke. The reason for this sudden localized clotting of blood is not known.

Knowledge of how thrombosis is initiated and propagated within atherosclerotic and normal blood vessels will allow design of new therapy. This knowledge can be gained by studies of the clotting process, the wall of the blood vessel and the dynamic properties of flowing blood.

The Council believes that studies of the mechanism of thrombosis would contribute to reducing the high morbidity and mortality resulting from atherosclerosis.

Thrombosis not only affects man's own vessels, but it also limits the usefulness of vascular prostheses and is a serious barrier to the development of long-term circulatory assistance or replacement devices (see page 15).

Coronary Heart Disease

Under the broad heading of atherosclerosis, atherosclerosis of the coronary vessels is the major problem. Two aspects in particular require special attention—myocardial infarction and sudden death.

Myocardial infarction irreversibly damages heart muscle, and, if extensive, causes heart failure, either during the acute episode or following recovery from the attack. Means to reduce the amount of damaged muscle would substantially reduce the threat of heart failure and reduce the disability following a heart attack.

One half or more of the deaths from coronary heart disease occur suddenly. Current evidence suggests these deaths probably result from arrhythmia (abnormal heart rhythm) or cardiac arrest. How to prevent or treat such events represents a major problem in heart disease today. If the patients likely to develop these fatal arrhythmias could be identified, many lives could be saved by appropriate preventive or resuscitative procedures.

The Council recommends broad studies, by a variety of approaches, of means to minimize the mass of irreversibly damaged tissue resulting from occlusion of the coronary vessels.

The Council recommends continued exploration of the electrophysiology of the heart in order to develop more effective antiarrhythmic drugs.

The Council recommends studies to identify the population at risk of developing arrhythmias so that prospective therapeutic trials aimed at prevention can be designed and initiated.

Hypertension

Hypertension can be controlled by a wide variety of drugs, but they must be taken continuously for the remainder of the patient's lifetime. Current treatment is empirical and only a few types of hypertension are curable because in only a few types is the cause understood.

> **The Council gives high priority to investigation of the causes of hypertension through studies of all the physiologic control systems that determine arterial pressure.**

Such knowledge will have two benefits: (1) it will allow development of specific treatments to replace the empirical ones now used; this is of particular importance because of the possibility of long-term side effects, as yet unrecognized, if patients must continue indefinitely on drugs, and (2), such knowledge may allow development of methods to cure hypertension.

Recent work has shown that control of high blood pressure by drugs substantially reduces the likelihood of strokes and heart failure, but a similar beneficial effect on the occurrence of heart attacks has not yet been demonstrated.

> **The Council recommends continuation of clinical trials to determine the effect of long-term treatment of mild-to-moderate hypertension on the incidence of strokes and heart attacks.**

Rheumatic Fever and Rheumatic Heart Disease

The relation between streptococcal infection and rheumatic fever is well established, and prevention of rheumatic heart disease is near attainment. To achieve this goal, continued efforts should be directed toward developing a vaccine for active immunization against streptococcal infection. Such a vaccine would eliminate the necessity for life-long treatment with antibiotics. It is also important to determine why rheumatic fever develops only in some people with streptococcal infections, why rheumatic heart disease develops in only a proportion of people who develop rheumatic fever and why it selectively damages heart valves.

> **Until the final goal of prevention is reached, emphasis must be placed on early recognition and treatment of streptococcal infections, on behavioral research into the motivation of parents and children to seek immediate diagnosis and to stay on continued long-term treatment programs, and on improvement of techniques to facilitate rapid culture of streptococci.**

Congenital Heart Disease

At the present time, surgical correction of most congenital heart defects is possible. The Council is convinced, however, that prevention of congenital heart defects should be an ultimate goal of the National Program.

> **The Council recommends an intensive interdisciplinary study of the neonatal heart and blood vessels and all aspects of the etiology and pathophysiology of congenital heart disease.**

Because the majority of deaths occur during the first days or weeks of life, early recognition and treatment are the essence of an effective program.

> **The Council recommends efforts be made to improve early recognition and facilitate prompt treatment of infants with congenital heart disease (see page 20).**

Heart Failure

Heart failure is a serious complication of heart attack which may develop during or after the attack; it is also an important manifestation or consequence of a variety of diseases affecting the function of the heart, including hypertension, and rheumatic and congenital heart disease.

Current treatment is still either empirical or directed at secondary manifestations, such as edema. New information is needed concerning cardiac function in order to design improved therapy for patients with heart failure, whatever the cause, and to investigate new methods of prevention.

> **The Council gives priority to studies of the contractile process and development of methods to improve the function of heart muscle, and to studies of the humoral, neural, and endocrine factors which are involved in normal and abnormal cardiac function.**

2. LUNG DISEASES

The Report of the Lung Diseases Panel testifies eloquently to the disparity between the large number of severe lung disease problems and the few basic biologic facts available with which to fashion relevant therapy and prevention. The Panel Chairman, in presenting his report to the Council, commented on this disparity: "Study of respiratory diseases has only recently moved

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out of the tuberculosis sanitaria." Until recently, most pulmonary research concerned the lung as a site for infectious disease. The first textbook of lung physiology was published as recently as 1955 and subsequently the lung was studied primarily as a gas exchanger. Only in the last five years has the lung been studied as an organ with specific problems and properties.

As a public health problem, lung diseases are very important:

- Asthma affects 9 million Americans and usually lasts for years.
- Emphysema and chronic bronchitis doubled in incidence between 1958 and 1967. In 1967 they cost the U.S. economy an estimated $1.2 billion. Unlike most other diseases, they continue to increase.
- Lung fibrosis and respiratory failure are now being recognized in larger numbers—due in part to improved techniques of recognition and in part to environmental factors. Mortality in respiratory failure approaches 40 percent.
- Hyaline membrane disease affects about 50,000 newborns annually. Due to recent research advances, the disease is usually diagnosed correctly but survival varies from 20 percent in the majority of hospitals to 80 percent in a few excellent centers.

In contrast to the great and increasing problems of lung disease, there is a dearth of basic knowledge about the lung. The Lung Diseases Panel Report details many basic questions about the normal and diseased lung which must be answered as soon as possible if reduction in morbidity and mortality of lung diseases is to be accomplished.

The Lung and its Biology

Faced with this large discrepancy between severity of disease and lack of basic knowledge, the Panel Chairmen responded with the following general recommendation:

> "The major missing element in those respiratory diseases which comprise the bulk of respiratory disease is knowledge of the cellular biology of lung tissue. Understanding of this area would lead to major advances in chronic bronchitis, emphysema, pulmonary fibrosis, immunologic lung diseases, respiratory diseases of children and respiratory failure. Hence, studies in this area are the number one priority. More rapid progress in this area would be made by the establishment of investigative units organized to explore these basic considerations."

> **The Council strongly supports the Panel's recommendation. The priority need is for basic research into the lung and its biology.**

Any other approach would be palliative and eventually would emphasize the status quo. Research now in progress is expanding rapidly in areas such as normal lung metabolism, function and development, study of lung cells, response of lung to air pollutants and the basic chemical nature of the elastic fabric of the lung which is lost in diseases such as emphysema. Because research in lung biology and lung diseases is only beginning to emerge, extra efforts must be made to attract and support good investigators—young and old—in this area. Otherwise, programs will be seriously understaffed and progress will be limited.

Emphysema and Chronic Bronchitis

> **The Council recommends that an attack be mounted on emphysema with major emphasis on an intensive effort to find the cause of this important disease.**

All possible causes should be identified and systematically studied or eliminated. Particular attention should be paid to the reaction of the lung to injury by physical and chemical agents, infectious diseases, metabolic diseases and reduced blood supply, and the mechanisms by which the lung defends itself. Advances in understanding the lung in emphysema, the principal clinical problem in pulmonary disease, will at the same time provide much basic data needed for further progress in other areas.

At all times, methods for early diagnosis and methods to prevent emphysema or halt its progress should be sought. As an example of a specific approach, programs designed to decrease smoking would have a major impact. The reduction of smoking in the young would be a preventive measure and at the same time would yield valuable prospective data on the effect of smoking on development of chronic lung and heart and blood vessel diseases (see also page 20).

Respiratory Failure

The Council believes that immediate improvement in the problem of respiratory failure is possible through increased emphasis on clinical studies, improved early detection, and demonstration of emergency services, especially intensive respiratory care research units. For the long-range attack on this problem, basic knowledge of the pathophysiology of the condition through animal study should be encouraged.

The development of an artificial lung to support adults and infants in respiratory distress is now underway. This effort should be vigorously pursued for such a device would provide both clinical benefits to patients and new capabilities in the research laboratory.

Immunologic Lung Diseases

Several lung diseases are a consequence of immunologic abnormalities. They include asthma, hypersensitivity pneumonitis, sarcoidosis and lung fibrosis. A rationale for treatment of immunologic lung disease will require an understanding of immunologic differences between various individuals and between the elderly and the young.

The Council believes that basic studies of the immunology of the lung are required.

Studies are needed to identify the causes of pulmonary fibrosis and sarcoidosis and to elucidate the role of infection in causing an asthmatic attack.

Lung Diseases of Infancy and Early Childhood

The Council concurs with the following Panel Chairmen's recommendation:

"Hyaline membrane disease and cystic fibrosis require the development of methods of early and prenatal diagnosis and the development of regional emergency care centers where meticulous and sophisticated techniques are available, including provision for rapid transfer of affected children to these facilities."

Prospective, controlled studies of infants likely to develop hyaline membrane disease are indicated (see page 20). Recent research offers an explanation of why infants born prematurely may develop this disease and provides methods for detection of risk prior to birth. As an immediate measure, prenatal detection and therapy must be evaluated and presently defined criteria for treatment must be standardized to assure optimal care and survival. Such studies can best be carried out in a small number of specialized centers of research. The concept of these centers is developed below (see page 30).

The goal of prevention will require basic understanding of the cellular biology of the developing fetus and the control mechanisms of fetal maturation. Furthermore, understanding of the basic mechanisms responsible for premature birth is essential in order to prevent premature delivery and thereby reduce the incidence of hyaline membrane disease. This disease demonstrates very well how ultimate control of disease rests upon the understanding of its basic cause.

Obstructive Lung Diseases in Infants and Children

The Council recommends studies to define the causes of upper and especially lower airway obstructive disease in children.

It is important to determine whether obstructive lung disease in children predisposes to the development of obstructive lung disease in adults. Investigations of croup and bronchiolitis should be directed toward determining their cause and developing methods for early detection and specific management. Emphasis should be on epidemiological and long-term follow-up studies.

In much the same way that the problems of infants with hyaline membrane disease might best be served by specialized centers of research, obstructive lung disease in children should also be studied in such centers.

Manpower Needs

The Panel pointed to manpower needs in the area of lung diseases. Because of the markedly increased emphasis on lung diseases and the magnitude of the clinical problems, the demand for trained manpower is greater than the supply. More than 200 vacancies for trained investigators and clinicians exist at present. This is one of the major examples of our failure to apply current technology consistently for every patient needing it. The limiting factor is quite simply the small national pool of trained and knowledgeable personnel. Plans for meeting these immediate and future needs must be implemented at once to prevent a critical shortage of manpower.

3. BLOOD DISEASES

The Blood Diseases Panel Report addressed three principal areas as follows:

- *Thrombosis,* with emphasis on two major aspects: (1) arterial thrombosis and its role in causing such serious and fatal complications of atherosclerosis as heart attacks and stroke, and (2) venous thrombosis and pulmonary embolism.
- *Hemorrhage,* with emphasis also on two major aspects: (1) the seriousness of uncontrolled hemorrhage, a major cause of morbidity and death, in a variety of conditions, such as after surgery or accidents or in cirrhosis of the liver; and (2) the hemophilias, inherited hemorrhagic disorders which have great socioeconomic consequences, on families with these diseases and on society generally, particularly on the blood resource system of the country.
- *Sickle cell anemia and related inherited disorders* of the red cell and its contained hemoglobin.

Many significant advances have been made in the treatment of certain thrombotic and hemorrhagic diseases; research discoveries have become part of everyday medical practice. Examples include anticoagulant therapy for patients with clotting problems and plasma concentrate treatment for hemorrhage in hemophilia. But many serious disorders cannot be prevented or treated effectively, or at times even diagnosed. For example, thrombosis may go entirely undetected until the clot or a piece of it breaks loose and causes a sudden catastrophe such as pulmonary embolism or gangrene of an extremity.

By the authority of the National Heart, Blood Vessel, Lung, and Blood Act of 1972, not less than 15 percent of the funds appropriated to the National Heart and Lung Institute shall be reserved for "programs respecting diseases of the blood." An important segment of the program relates to sickle cell disease. Initiation of this activity was accompanied by specially earmarked funds. These funds, together with sizeable annual increments in the funding level, have made it possible to implement an effective sickle cell disease program which should continue. Other disorders of the blood likewise disable or cripple many thousands. These diseases could be expected to yield to intensified attack, sparing patients pain while conserving the nation's blood resources as well. Concentrated research effort directed toward specific blood diseases is essential and overall program balance is needed. The following paragraphs present the Council's recommendations in the area of blood diseases.

Pathogenesis of Blood Diseases

> **The Council concurs with the Panel's recommendations that a major effort should be made in research on the pathogenesis of thrombosis (see page 10).**

> **The Council recommends that a major effort should also be made on the pathogenesis of hemorrhagic diseases and red cell diseases and the biologic mechanisms underlying these disorders.**

Basic knowledge is urgently needed on the mechanisms of blood clot formation, thrombus formation on atherosclerotic plaques, and prevention of thrombosis. Treatment of the thrombotic disorders, based on present knowledge, can be only partially effective at best.

Additional basic information in molecular genetics could completely alter the approach to treatment of the inherited blood diseases, hemophilia and sickle cell anemia. For example, if one could "turn on" the latent capacity of the sickle cell anemia patient to produce normal fetal hemoglobin, the scourges of this disease could be largely overcome.

Clinical Trials of Antithrombotic Agents

There are many drugs today which may prevent or dissolve clots, such as the coumarins, heparin, the thrombolytic agents, aspirin, and certain snake venoms. Special attention is required in the selection of appropriate drugs for clinical trial.

> **The Council believes that clinical trials of promising new drugs should be conducted.**

The Council agrees with the Panel Chairmen's recommendation that aspirin and low dosage heparin as antithrombotic agents are the most promising candidates for testing at this time. Other possible agents are the antithrombotic snake venoms and the thrombolytic agents. However, end points for determining efficacy may be especially difficult. Careful design of the studies must take into account rigorous assessment of feasibility, present state of the art, and cost versus probable knowledge to be gained. Also, the problems that may be encountered in translating the findings to general medical practice should be considered before starting any clinical drug trials.

Development of Nonthrombogenic Surfaces

Completely satisfactory materials for heart valves, artificial organs, and other prostheses are not available. All of those presently in use stimulate the formation of thrombi.

> **Greater emphasis, in both applied and basic research, should be given to nonthrombogenic surfaces.**

Research is needed on the surface characteristics of biomaterials, as well as on the normal lining endothelium of the blood vessels. The former are thrombogenic, the latter is not. Elucidation of this difference could result in development of completely nonthrombogenic surface materials and of ways to avoid thrombi in thrombosis-prone diseased vessels.

4. BLOOD RESOURCES

The availability of an adequate supply of high-quality blood and blood products is essential for effective treatment of many diseases. The report of the Blood Resources Panel deals with four important areas: A National Blood Bank System, Blood Component Therapy, Hepatitis, and Transplantation Immunology.

In the assessment of priorities and opportunities in the blood resources area, a number of factors were considered, including the following:

- The magnitude and strength of the diverse but uncoordinated blood banking system which presently functions to meet most medical situations, but whose many defects could be overcome with a well-coordinated national system;
- The inadequacy of present blood fractionation methods and the need for vigorous attention to more efficient isolation of the many cellular and plasma components of the blood; and
- The fact that rapid advances are being made in understanding hepatitis, including serum hepatitis, but there is still no way today to ensure that blood from a given donor will not transmit the disease.

A National Blood Bank System

A national blood bank system should be developed from existing blood bank resources of the country so that a coordinated system based on regions would eventually result. Part of this effort would include the establishment of a national blood data center and a continuing campaign on the national level for recruitment of blood donors to ensure an adequate supply of blood for the country's needs. The system could eventually include preservation and storage of organs and tissues for transplantation.

> **The Council believes a coordinated blood bank system at the regional and national level is highly desirable, provided that full utilization is made of the existing resources in present blood banking organizations.**
>
> **The blood bank system should include the supply of blood, its processing, distribution and utilization. It could also included tissue typing and organ preservation but not other aspects of transplantation.**

The role of the National Heart and Lung Institute should be to facilitate coordination and further development of present resources into a total national program. No single rigid pattern of organization would likely meet the diverse geographical requirements of the country.

> **The deficit in trained personnel deserves special attention. Training of professionals in the blood banking field is very limited in this country and is inadequate to meet the demands for qualified physicians to staff the blood banks of the nation.**

Blood Component Therapy

Blood component therapy, to be fully effective, requires improvement in blood cell preservation and plasma fractionation, so that the many important components of blood such as platelets, immune globulins and antihemophilia factors can be fully recovered for treatment purposes.

> **The Council emphasizes the need for improved therapy using blood cells, particularly white cells and platelets, and plasma protein components.**
>
> **Specialized centers of research in blood and blood resources should be established.**

Competition for the specialized centers should be on a broad base and not limited solely to regional or national blood centers. One or more of these centers should contain pilot plants to develop and test new methods for plasma fractionation. Fundamental research in immunology, immunogenetics, and other aspects of transplantation biology could be carried out in such specialized centers although clinical trials of organ transplantation would not be appropriate until fundamental new knowledge is available.

Hepatitis

Hepatitis, which includes hepatitis B transmitted by blood transfusions, continues to be an important public health problem, requiring a coordinated attack.

> **The Council recommends continuation of studies aimed at better understanding of the virus, improvement of tests for detecting carriers of the disease, and development of a vaccine.**

Transplantation Immunology

Transplantation immunology requires continued research and development if wider and fully successful use of organ transplants in the heart and blood vessel, lung and other areas is to be realized.

General Comments

In the operational area of blood banking, the role of the National Heart and Lung Institute should be that of catalyst for the system, through collection of data, support of research and development in the blood area, and provision of a meeting ground and advisory system to the purveyors of blood and blood derivatives in the country.

Motivational research is needed to understand more fully the reasons that prompt people to give blood, in order to place the blood donor recruitment system on a sounder basis (see page 17).

There must be a continuing program for professional and public information and education regarding blood and its most effective utilization. In addition, special efforts must be made to enlist the interest of the scientific community in the blood resources field so that more attention is given to important research and development leading to better utilization of our blood resources (see page 19).

5. GENERAL NEEDS FOR ALL AREAS

Certain common needs are shared by all four areas—heart and blood vessel diseases, lung diseases, blood diseases, and blood resources—discussed in this report. Among these are information gained from studies of genetic factors, animal models and human motivation.

Genetics

There is firm evidence that hypertension is, in part, an inherited disorder. Atherosclerosis may also have genetic determinants. Hemophilia, sickle cell disease and thalassemia are definitely inherited disorders. In a small proportion of patients with emphysema (those with the alpha$_1$-antitrypsin deficiency), a genetic defect is present.

It is clear that knowledge concerning genetic factors is necessary not only for understanding how diseases develop but also for the design of specific treatments. Such information could come from study of human populations as well as from study of animal models of human disease.

> **The Council recommends that a strong and positive program of genetic research and counseling be established to help decrease heart, blood vessel, lung and blood diseases of genetic origin.**

Animal Models

Use of animal models can have important impact on understanding disease and often may be the only available research approach. For instance, recognition of a naturally occurring hemophilia in dogs allowed identification of the causes of this disease. Development of models of thrombotic and other hemorrhagic diseases is needed. Animal models of hypertension, developed by a variety of different methods, have shown the multifactorial nature of this disorder and have improved the development of drugs for treatment. Our understanding of atherosclerosis would be much advanced by the availability of a primate model which would allow application of current knowledge in design of methods of control and which could be used as new leads develop. Similar benefits would accrue from the development of animal models of lung diseases.

Motivational Research

Very little is known about the factors that motivate individuals to help or hinder control of their health problems. For example, cigarette smoking is known to cause lung disease; the information has been widely disseminated, but cigarette usage has risen. Hypertension is now controllable by drugs, yet a substantial number of patients do not seem willing to continue the necessary long-term treatment. Some types of hyperlipidemia can be easily controlled by simple dietary modification, but many people either will not or cannot make the necessary changes in food intake. An understanding of what motivates people to donate blood could lead to a stable blood procurement system.

Information gained from research in the past 25 years has begun to move medicine away from care of the crises of illness toward the maintenance of health. In the former situation, the ill patient played little role, but in the present situation, his motivation to help himself is the vital, and often lacking, ingredient. If this National Program is to be successful, much new information will be needed concerning the mechanisms of motivation for self-help or self-destruction.

IV. EDUCATION, CONTROL AND PREVENTION

The Council believes that, in response to Section 414 of the Act, the National Heart and Lung Institute should implement a program of education for control and prevention of heart, blood vessel, lung and blood diseases.

EDUCATION

> In the area of public and professional education, the Act provides particular opportunities for progress and vigorous efforts should be made. A few examples include research into the best means for continuing public and professional education; provision of information to the Congress, the public and the professional community; and support of the educational efforts of private agencies.

Real practical progress could be made by inclusion of formal mechanisms for education in each National Research and Demonstration Center (see page 30). An organized effort for scientific communication between investigators, centers, the National Heart and Lung Institute and the community should be strongly supported.

Section 413(d) of the Act stipulates that the Director of the National Heart and Lung Institute shall appoint an Assistant Director for Health Information Programs for the purpose of providing the public and the health professions with health information concerning heart, blood vessel, and lung diseases. In the wording of the Act, blood diseases and blood resources are omitted.

> The Assistant Director should stimulate a program of research on improving the effectiveness of education in heart, blood vessel, lung and blood diseases. He should also be responsible for coordinating educational and informational programs of the National Heart and Lung Institute with voluntary health agencies such as the American Heart Association, American Lung Association, American College of Chest Physicians, American College of Cardiology.

The Council suggests that the Assistant Director involve the appropriate voluntary health agencies in these efforts because of their longstanding interest and ongoing programs of public education and information.

> Furthermore, the Assistant Director's activities should be legally expanded to include education in regard to blood diseases and blood resources.

A major effort must be made to formulate suitable programs for encouraging the public to develop habits that may be of benefit in preventing the development or progression of heart, blood vessel, lung and blood diseases. The public and professional mass education techniques now used to alter health practices are notoriously ineffective. They should be replaced by an effective program of education regarding the pre-

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vention of disease and the importance of early detection and treatment. Sociologists, behavioral scientists and psychologists should be asked to assist in developing and conducting studies that focus on motivation and methodology.

CONTROL AND PREVENTION

The Council believes that a limited number of demonstration projects should be developed to:

- **Test methods for the education of the public and professional community;**
- **Demonstrate the feasibility and advantages of community and regional care systems for specific diseases;**
- **Demonstrate the clinical applicability of the results of research;**
- **Develop effective prototype community efforts for improved detection, diagnosis, treatment and follow-up of persons with heart, blood vessel, lung and blood diseases, including training of allied health professionals, many of whom may come from the community; and**
- **Investigate factors important in public acceptability of research findings.**

These programs should have a primary research objective, should be time-limited, should provide only those health care services necessary to the project and should be reported in media designed for clinicians, health workers and the public. In all instances, there should be cooperation with existing health resources so that procedures once generated and demonstrated to be effective can be incorporated into ongoing health programs.

The following are examples of demonstration programs which are already under way or should be started in the near future.

- The early detection of hypertension, treatment by drugs and control of long-term complications is already under way. This involves public education, clinical application of research findings, and provides for further research into the disease process.
- The benefits of very early diagnosis and treatment of congenital heart disease should be demonstrated. This would be based on intensive public and professional education regarding the benefits accruing from very early diagnosis and acceptance of care at a single regional center. The project would also bring increased numbers of early diagnosed infants into prospective studies of clinical management.
- The prenatal diagnosis of hyaline membrane disease should be demonstrated by a regional center. Mothers in whom the diagnosis has been made should deliver in the regional center where all available, specialized, and research-proven techniques for management of the disease can be applied. Mortality of affected infants should be very much reduced by this intensive early care.
- An effective means to control smoking needs to be developed and demonstrated. Despite the widely disseminated knowledge that smoking is implicated in heart, blood vessel and lung diseases, as well as cancer, the use of tobacco in this country is increasing. Overall data for all diseases resulting from smoking indicate that the average smoker shortens his life by approximately four years, while some categories of smokers, such as those who begin at an early age and smoke several packs of cigarettes a day, may shorten their lives by a statistical average of as much as eight years. A program to motivate people to stop smoking would be entirely one of education but one which would require full community support and participation. The Council strongly recommends implementation of such a program in conjunction with other Federal and non-Federal agencies.

When Federal funds are used for demonstration projects, care must be taken to avoid replacing local support. Such projects, by their very nature, are time-limited and Federal support ultimately will be withdrawn. Each project should be designed from the outset to include a critical evaluation of its worth and effectiveness. Each is thus a research project investigating the feasibility of translating research results into reality in the health care system. When this translation is complete, local sources of support will be required for continuation of the program.

INTERAGENCY TECHNICAL COMMITTEE

Section 416 of the Act provides for establishment of an Interagency Technical Committee, with the Director of the National Heart and Lung Institute as Chairman, responsible for coordinating those aspects of Federal programs that deal with heart, blood vessel, lung and blood diseases and blood resources.

Many agencies, public and private, have their own programs of research, education or public information in these areas. Of the Federal agencies, the most important are the National Institutes of Health (NIH), Health Services and Mental Health Administration (HSMHA), Food and Drug Administration (FDA), Veterans Administration (VA), Department of Defense (DOD), National Aeronautics and Space Administration (NASA), Atomic Energy Commission (AEC), Environmental Protection Agency (EPA), Department of Transportation (DOT), Social and Rehabilitation Services (SRS), Social Security Administration (SSA), Department of Agriculture (DA), and National Science Foundation (NSF). All are represented on the Interagency Technical Committee.

For an effective National Program, the Council believes that all appropriate efforts of Federal agencies should be coordinated by a committee with responsibility to:

- **Know the full extent of the effort presently supported by all agencies, and that planned for the future;**
- **Avoid needless, unproductive overlap of effort;**
- **Identify neglected fields that deserve considerable expansion of effort;**
- **Provide the best scientific advice on large cooperative programs before they are approved and launched; and**
- **Assure all agencies rapid access to knowledge developed in all programs. The Council hopes that private agencies will also participate in this national effort to exchange information and coordinate programs.**

The National Heart and Lung Institute should ensure that, through the Interagency Technical Committee and other means, advances resulting from research in heart, blood vessel, lung and blood diseases are incorporated into other national health service programs; for example, emergency services that emphasize cardiac and pulmonary resuscitation should incorporate research advances in electrophysiology and resuscitation.

V. SCIENTISTS AND THEIR SUPPORT

To accommodate the needs for both fundamental and mission-oriented research, the National Heart and Lung Institute requires a wide variety of support mechanisms suitable to a wide variety of investigators. Some investigators do their best work alone, others do best when working in small groups; still others are most productive when they have the stimulus that comes from frequent exchange of ideas in a large interdisciplinary center. Some investigators are highly imaginative and generate their own ideas, and some are less innovative but are highly productive in following leads of others or working in collaborative programs with carefully designed protocols. Whatever the system for the support of research, it must both favor the imaginative, innovative investigator and provide for flexibility to explore new leads whenever and however they are identified.

The recent fluctuations in Federal support of research have, by lowering morale, made careers in biomedical science far less attractive than they were some years ago and thus have been costly to a sustained research effort. The assurance of more positions with more stability will do much to attract and keep brilliant and creative scientists in heart and blood vessel, lung and blood research.

RESEARCH PROFESSORSHIPS

The Council acknowledges the considerable stimulus to investigators that comes from close association with medical and graduate students and from observation of patients. But it also believes that the rapid advance of the National Program requires that more senior scientists dedicate 80 to 90 percent of their time to research. Therefore, the Council proposes that stable positions should be made available for senior investigators who wish to devote their main efforts to research on the heart, lungs or blood. Further, long-term national goals will be achieved more quickly if every school of medicine has such a stable position to offer a scientist who can develop a vigorous heart and blood vessel, lung or blood research program.

> **The Council recommends, as a very effective means of accomplishing national goals, that the National Heart and Lung Institute should establish a Research Professorship in every medical school in this country. Approximately $10,000,000 a year should be appropriated, and allocated, for this purpose.**

The Council envisions this as stable support, through a long-term grant, of a *position* in each school of medicine rather than the support of a specific research project. An established senior investigator would be named by the school but must be acceptable to the National Heart and Lung Institute. During his tenure in the position, he would be freed from all but minor responsibilities of teaching, administration and clinical care.

The concept of the Career Investigator is one used quite effectively by the American Heart Association (AHA) since 1951. Its philosophical approach toward the support of research has been one of supporting people rather than their projects in the conviction that the decrease and the eventual elimination of cardiovascular disease can best be achieved through a stable, consistent research effort by the most talented and productive minds available. The record of achievement by the recipients of AHA Career Investigator awards bears out the soundness of that philosophy. The AHA has found that the work of Career Investigators is cited more than twice as often in scientific literature as the work of "top candidates" who were nominated for the investigatorship but did not receive it. Further, the AHA Career Investigators, now freed from responsibilities unrelated to their career goals, have attained a level of productivity considerably higher than that before accepting the award. The award has not removed their work from peer review since they must secure much of their research expenses through national competition. In addition, the Career Investigators have an impressive record for teaching students and training young scientists. The Council believes this is a program which should now be greatly expanded with the support of the National Heart and Lung Institute.

The Council strongly urges that a grant be awarded to each medical school in this country to create these positions. Each initial grant would be for a 10-year period, renewable for additional 10-year periods. The grant should include full salary of an established investigator at either the professor or associate professor level. In some schools it may be necessary to support this position at a salary level above the scale of the institution if an investigator of high quality is to be obtained. It is further recommended that the grant should include a full salary for a research fellow and for a technician to work with the investigator; plus $15,000 a year for partial costs of their research. The average amount for each unit in FY 74 would be $75,000 plus an additional amount for indirect cost allowance. Funds should also be made available for initial renovation of space and purchase of equipment if necessary during the first year of a new incumbent. The total funds required would be approximately $10,000,000 a year. The Research Professor, like the Career Investigator of the American Heart Association, would be expected to compete for additional research support, as needed, through other mechanisms, and these generally require competitive scientific review.

Each medical school would thus have assurance of stable funds for a senior research position so that it could actively recruit a scientist to fill it (although funds would not be released until a school has nominated an acceptable candidate).

Institutions should have the widest possible latitude in selecting a nominee. He could already be a member of the faculty of that school or could be recruited from elsewhere; he could hold an M.D., Ph.D., or other appropriate postdoctoral degree. He could work in a basic science or clinical department or both. Although his field of research at the time of his appointment would be in the heart and blood vessel, lung and blood area, broadly considered, he would be free to change direction within the field. The Research Professor would commit all of his effort to research except for a small amount to be spent in related teaching or training.

A candidate accepted for a position of Research Professor would hold the post only as long as he continued to devote his main energies to research. If, for any reason, the recipient left the institution, he could not transfer the award to his new school. If he accepted responsibilities that decreased his commitment to research, he would no longer be eligible for the award. If, at the end of the grant period, a peer group found him to be unproductive, he would not be eligible for another term. Under these circumstances, the school would be required to nominate a new candidate. The funds would not be available to the school when the position was not filled, but would be released upon acceptance of a new candidate by the National Heart and Lung Institute.

This program, designed to provide long-term stable support, would require a long-term commitment on the part of the National Heart and Lung Institute. But it would also require a considerable commitment on the part of the medical school, which would be expected to provide space and assurance of stability of appointment for the recipient.

There are a number of advantages of making such an award to each school. It would at once be a national program, since the awards would be geographically distributed throughout the country with each school having one such award. Further, the promise of stable and adequate support for a senior research position would help a smaller school with limited resources to attract a competent investigator who would then become the nucleus there for an expanded research effort on heart, lungs, or blood. This could well be a means of upgrading schools which at present have difficulty in competing successfully for National Heart and Lung Institute or other research support. At the same time, the program should have a beneficial effect on teaching medical students and training interns and residents in areas related to the heart and blood vessel, lung and blood field.

PROFESSORIAL RESEARCH GROUPS

The Research Professorship described above would assure support of a minimal research unit in each school for an individual scientist who wishes to devote his main energies to research. But to achieve the goal of conquering the diseases of the heart, lungs and blood, many more talented, imaginative men and women must be induced to enter and stay in careers in research related to these diseases. Universities, hospitals and private research institutes do not have the financial resources to pay the salaries of these additional research scientists and their support can come only from the Federal Government.

> **As a means of expanding the number of stable positions for creative scientists without draining the now-limited financial resources of universities and other private organizations, the Council recommends that $15,000,000 a year be allocated to the National Heart and Lung Institute for the support of Professorial Research Groups, each consisting of several competent investigators. Fifty such units should be established at an average cost of $300,000 per year; 40 should study disorders of the heart and blood vessels and/or lungs and 10, disorders of the blood.**

Professorial Groups have been supported for some years by the Medical Research Council of the United Kingdom as a means of attracting talented scientists into careers in medical research and of stimulating or expanding research in certain selected fields of national need; the United Kingdom program has been a very successful one.

The Council proposes that a grant to support a group usually should include full salary for a professor (who would be the director of the unit and would be assured of long-term support from the grant) and three associate professors or assistant professors. The grant should also include salaries for three technicians and approximately $50,000 a year for partial research expenses of the laboratory. With the addition of appropriate indirect costs and allowance for a degree of flexibility to compensate for local conditions, each unit would cost approximately $300,000 per year. Groups would be expected to obtain additional support as needed through other mechanisms. Grants for Professorial Groups would not be reserved for each school of medicine, but would be awarded on a competitive basis and only after competitive scientific review. They would be awarded for seven years, and should be renewable for seven-year periods.

The director of the group may be associated with a university, its medical schools or hospitals or a nonprofit research institute; he may hold the M.D., Ph.D. or other appropriate postdoctoral degree. He may be a member of a basic science or clinical department or of both and his application may request support for either basic or clinical research or both. Important considerations in its review would be the excellence of the proposed research program, its relation to the solution of heart and blood vessel, lung or blood problems, its long-term nature and the commitment of the group to devote all of its time to research for the period of the grant, except for a small amount that may be spent in related teaching and consulting activities.

A grant for a Professorial Research Group differs from one for a Research Professorship in that the former is an award to a small group of scientists who propose a specific research program and the latter is an award to a school of medicine to support a research professor. The grants are similar in that each has a goal to attract and keep competent scientists in full-time research by providing long-term and full support of professorial salaries.

RESEARCH CAREER DEVELOPMENT AWARDS AND SPECIAL RESEARCH FELLOWSHIPS

Phasing out the current programs through which the National Heart and Lung Institute pays the salaries of 200 established scientists who now devote almost full-time to research important to the National Program could diminish the national research resources by 200 scientists.

The Council urges that the Administration find an acceptable way of restoring these stipends and permitting important research to continue.

EDUCATION OF YOUNG SCIENTISTS

The Council believes that a critical need *now* for long-term success of the National Program (i.e., prevention and elimination of diseases of the heart, blood vessels, lung and blood) is recruitment and training of young scientists.

The Council sees no way to attain the long-term goal without the means to recruit talented young men and women and to provide excellent training for their research careers. These scientists-in-training (now called pre- or postdoctoral Research Fellows or Trainees) are absolutely essential to the Program for several reasons:

- They are needed to replace present investigators who die, retire or change careers.
- In certain long-neglected areas (e.g., lung disease), there is such a shortage of scientific personnel and scientist-teachers that a national program in research and education must limp along until a large number of young scientists is recruited and trained. The Lung Diseases Panel has emphasized that a diversity of scientists is needed—not only medically trained scientists but also basic scientists in the areas of physiology, biochemistry, biophysics, genetics, immunology and epidemiology.
- Research Fellows and Trainees are required for the actual conduct of much of the National Heart and Lung Institute research now in progress—research supported by research project grants, program project grants and specialized centers of research.
- Although less readily understood by laymen, an equally important reason for support of Research Fellows and Trainees is the stimulus provided to senior scientists by the merciless questioning of inquisitive, critical, young men and women who have different backgrounds and different scientific prejudices than their mentors. New blood brings new questions and new ideas; turnover of Research Fellows and Trainees every two to three years represents an inexpensive and effective way to maintain and increase scientific productivity of senior staff.
- An effective way of establishing communication and cross-fertilization among research groups working in different parts of the country is the training in one institution of postdoctoral Fellows who subsequently will work in another.

The Council strongly believes that the education of young medical scientists is clearly a national responsibility.

- Young scientists are a valuable national resource and their development is a national obligation since their work benefits all of our people in all 50 states. No one would ever consider the possibility that each state and each community should make its own medical discoveries and reserve these for its own residents. New methods of treatment discovered in Mississippi are applicable at once to California; new diagnostic methods devised in Massachusetts are applicable immediately to Alaska.
- States and regions vary greatly in their ability to support medical research and training. National support is needed to prevent discrimination because of economic, geographic, minority or other factors.
- Unlike medical practitioners who usually practice in the state where they have received their medical or postgraduate education, medical scientists who are trained in a limited number of centers of excellence more often spend their research and teaching careers in another of our 105 medical schools in another of our 50 states.

The Council unanimously and strongly urges that funds be allocated to the National Heart and Lung Institute to train young men and women for research careers.

The Council has considered the advantages and disadvantages of several mechanisms that have been proposed. Four alternatives are identified.

- *Loans for Trainees*. This mechanism has the advantage of little or no cost to the Federal Government but the disadvantage that it cannot possibly meet the special needs of the National Heart and Lung Institute. It is unrealistic to believe that the most innovative and creative young men and women will also be the most idealistic who will elect to accumulate an additional debt of $20,000 to $30,000 to obtain two to three years of research training (after a long period of financing their college and professional education) when the alternative is to *earn* over the same period $24,000 to $36,000 as hospital residents. A loan system will surely result in exclusion of practically all economically disadvantaged people from advancing their careers in medical science at a time when the Federal Government has a policy of affirmative action.

  There is no reason to believe that those who *do* have the independent financial means to obtain training in science will favor careers in cancer or heart, blood vessel, lung and blood research at a time when the conquest of cancer and heart disease has been assigned top national priority. To assure success for the Program, financial incentives must be added for training young scientists.

- *Stipends for Research Fellows and Trainees*. This mechanism would require allocation of sufficient funds to the National Heart and Lung Institute to award Traineeships or Fellowships, the number in various areas of research to be determined annually by the National Heart and Lung Institute with the objective of meeting the needs of the National Program. Awards would be made after competitive review to individual applicants on the basis of their past record, promise for future achievement and acceptability by an institution and scientists judged by the National Heart and Lung Institute to have outstanding capability for research training.

  Important advantages of the program are that it provides diversity of training opportunities and that the presence of Research Fellows in the diverse research laboratories acts as a catalyst to increase the quality of research generated in the laboratories. A disadvantage is that broad scientific training is not a required part of the program.

- *Research Training Program*. The Council at its March 1972 meeting agreed with the Administration that important modifications were needed in its Graduate Training Programs. The Council decided that the National Heart and Lung Institute needs a program designed to train those research scientists required to achieve the goals of its National Program and that the number and types of Research Trainees should be reviewed periodically.

  Such a program has the disadvantage of costing more in that it requires support for *programs* (faculty and supporting staff) as well as for *stipends*. It has the advantage that the training program itself is subject to competitive scientific review to ensure that Trainees receive total scientific education and training needed to equip them best for future research careers.

- *Salaries for Scientific Staff*. In the event that none of these programs is funded adequately, the Council has no alternative but to request additional research funds to pay for scientific staff to replace those lost by not paying Trainee stipends. It has not been generally recognized that each pre- or postdoctoral Research Trainee or Fellow spends at least 30 to 40 hours per week in research ("on the job") training under the supervision of a senior scientist. There are now 995 full-time Fellows or Trainees and 350 part-time Trainees supported by National Heart and Lung Institute Research Fellowships and Graduate Training Grants; of these, 675 are full-time Trainees in research and 670 are part-time. Elimination of these reduces by 675 the number of full-time scientists and by 670 the number of part-time scientists now engaged in heart and blood vessel, lung, and blood research. It is essential to replace these with research assistants to maintain the present level of research activity in the laboratories where Trainees now work.

In considering mechanisms for funding, Congress should remember that the last mechanism noted above will increase indirect costs from 8 percent on each stipend (allowed on Training Grants) to an average of approximately 50 percent on each salary (allowed on Research Grants).

EFFECTIVE UTILIZATION OF SCIENTIFIC MANPOWER

Although the Council is justifiably concerned about production of scientific personnel for research programs in future generations, it is equally concerned with full and effective utilization of the presently trained scientific manpower. It is clear from the number of research grant applications received by the National Heart and Lung Institute each year, as well as from the number of these applications that are considered to be meritorious but cannot be funded, that there is a large body of scientific manpower now available to perform more heart and blood vessel, lung and blood research than can now be funded. Many of the proposals already made in this Council report are aimed at full utilization of this manpower while also achieving the goals of the National Program. However, most of the mechanisms that have been innovated in the last few years for increasing the rate and quality of research productivity have favored support of larger programs of research, all of which have a tendency to increase the support of research groups in medical schools and other medical centers that are already among the better supported. There is justifiable concern on the part of many of our smaller institutions that the present trend can redistribute research manpower in such a way that it leads to weakening of research in many of our less affluent medical schools and centers. Furthermore, because the less affluent schools train a significant proportion of the doctors of our nation, the presence of good research programs in these schools will have double pay-off: first, for the research results themselves and, second, for their value in enhancing the quality and quantity of the training programs in all sectors of our nation.

> **The Council recommends that a committee be formed, composed at least three-fourths of persons from smaller institutions, that will report annually to the Council on ways and means of increasing the participation of the smaller and less affluent medical schools and certain other medical institutions in the national heart, blood vessel, lung, and blood research effort.**
>
> **The Council further recommends that such institutions be offered assistance in the development of their programs.**

Medical schools and other institutions whose ratio of Federal to local support is low should have the privilege of requesting an annual visit from an ad hoc committee chosen and detailed by the National Heart and Lung Institute. The purpose of the visit would be to help the institution select from among its personnel those who are worthy of research support and to establish a plan and a budget for funding their research. The committee shall then submit this for consideration and scientific review by a consultant panel responsible to the National Heart and Lung Institute. This panel, in turn, shall recommend a budget for support of specific research projects in such institutions. Projects thus supported, however, must have priority ratings that would be fundable in competition with other research and program project grants supported by the National Heart and Lung Institute.

VI. FISCAL MECHANISMS: GRANTS, CENTERS, CONTRACTS

Many fiscal mechanisms are available for implementation of a National Program. The ways in which they are used must be responsive to the goals, and must permit a planned and systematic exploration of promising avenues and the rational assignment of priorities. At the same time, a degree of flexibility must be maintained and the mechanisms of support must foster creative innovation and allow for new and unplanned breakthroughs. No one fiscal mechanism will achieve these goals. In this section, the Council reviews the present methods of support and makes specific recommendations.

RESEARCH AND PROGRAM PROJECT GRANTS

> The Council strongly endorses the current research grant programs that support investigators who generate their own ideas and can pursue these ideas independently; their research may be basic or clinical.

The Council gives its highest priority to support of independent research that may lead to more basic knowledge in all areas related to diseases of the heart, blood vessels, lungs and blood, even though the connection may not be immediately apparent. Increased funding for research projects and program projects initiated by investigators is essential to this effort.

The FY 73 National Heart and Lung Institute budget of approximately $100,000,000 for such grants should be increased by 25 percent in FY 74, and by an additional 25 percent in each of FY 75 and 76. In FY 77 and beyond, the level of support of these programs should be maintained in terms of actual buying power of the dollar. The increases are needed for the following reasons:

- The actual amount of research "purchased" with National Heart and Lung Institute funds has *decreased* year by year as salaries of scientists and their supporting staffs, costs of supplies, services and equipment, indirect costs of research and fringe benefits have risen far beyond the increase in funds allocated for research project and program project grants;
- Many approved research projects that may be important to heart, blood vessel, lung and blood research have not been funded; and
- The National Program requires an influx of young and senior scientists not now working on National Heart and Lung Institute programs.

When a research project or program project receives a priority that places it within the top 25 percent of grants approved in competitive scientific review, an award of up to seven years should be made (unless inappropriate due to the nature of the research project) to provide stability of support. Similar long-term awards should be made whenever the nature of approved research requires a long period to obtain essential data.

SPECIALIZED CENTERS OF RESEARCH (SCOR's)

The National Heart and Lung Institute recently initiated a program of support of Specialized Centers of Research to speed the development of new knowledge essential for improved diagnosis, treatment and prevention of specific diseases by focusing resources, facilities and manpower on particular problems. The diseases and the specific problems for investigation in a SCOR are first identified by the National Heart and Lung Institute. Applications are then invited and reviewed. Funding is by the grant mechanism. The effort in most SCORs is a multifaceted one and includes both basic and clinical research. SCORs have been activated in arteriosclerosis, hypertension, thrombosis and pulmonary diseases.

SCOR activities are coordinated by the National Heart and Lung Institute staff. Active cooperation among Centers is expected, and in fact required, to speed the dissemination of new knowledge. The Council endorses the concept of the Specialized Centers of Research as an effective means of mounting a National Program in certain disease categories.

> **The Council recommends that additional Specialized Centers be supported for study of other clinical problems (such as heart failure, and diseases of the heart, lungs and blood in the newborn) and for improving national resources (such as blood banking) when there is a reasonable chance that the initiation of a SCOR will result in more rapid acquisition of specialized knowledge and its application.**

NATIONAL RESEARCH AND DEMONSTRATION CENTERS

Section 415 of the Act states that the Director of the National Heart and Lung Institute may establish centers for basic and clinical research into, training in, and demonstration of, advanced diagnostic, prevention and treatment methods (including methods of providing emergency medical services) in heart, blood vessel, lung and blood diseases. Such centers have yet to be established. There could be as many as 15 for heart, blood vessel and blood diseases and 15 for lung diseases.

Centers should not necessarily attempt to encompass all the provisions of the Act. For the purpose of the National Program, the emphasis should be on the acquisition of new knowledge. To this end, they may be centers for basic research utilizing many scientific disciplines but devoted to the study of one area (e.g., pathogenesis of atherosclerosis or thrombosis, biology of the normal lung). Or, they may combine both basic and clinical studies, serving as an important mechanism for bridging the gulf between fundamental research and application of results to patient care. Although centers of the latter type may be concerned with research into improved methods of diagnosis and treatment, they would carry on patient care only insofar as it relates to their specific research efforts. After improved methods of diagnosis and care are developed and demonstrated by such centers, the Interagency Technical Committee would be an appropriate mechanism through which broad clinical applications could be planned.

The idea of the interdisciplinary, multidepartmental, comprehensive center is an important one in planning how best to fulfill the requirements of the Act. Such centers provide a critical mass of scientists in many disciplines. This facilitates sharing of ideas and knowledge, hastens the exploration of new ideas, provides for critical evaluation of ongoing work and creates an ideal setting for training future biomedical scientists.

In addition to engaging in broadly based and intensive scientific endeavors, a center should have a keen sense of responsibility in regard to professional and public education and information and of commitment to the overall purpose of the National Program. An education and information program, insofar as possible, should be an integral part of each center's activities. The medical profession should know of the center's scientific activities and the new knowledge these generate. The public should be kept informed on matters relating to health and control of heart, blood vessel, lung and blood diseases and the center's contributions to these areas of knowledge.

> **The Council agrees that establishment of such comprehensive centers would be an appropriate mechanism to meet the goals of the National Program.**

Before activating any centers, however, the National Heart and Lung Institute should carefully consider such matters as optimal size and location; the initial number to be established; establishment of additional centers according to changing needs of the National Program; avoidance of a rigid, organizational plan to which each center must conform; a mechanism for review and evaluation of overall achievements, strengths and weaknesses; a mechanism for phasing out unsuccessful centers; the effect on other programs of the National Heart and Lung Institute caused by allocating large sums of money to centers; and the effect on national distribution of scientific manpower that might be caused by establishing centers.

The Council believes that administrative arrangements should be determined individually according to each center's relationship with its parent organization and its unique research support needs.

CONTRACT-SUPPORTED RESEARCH AND DEVELOPMENT

Until recently, the National Heart and Lung Institute has supported research largely by grants awarded (after competitive scientific review) to scientists to work on problems *they* judge to be important (investigator-initiated grants), whether in basic or clinical fields. Recognition that sole dependence on investigator-initiated programs may result in neglect or under-emphasis of some scientific areas has led to the use of contracts to support research identified as essential to national needs by Institute staff, or its appointed consultants, committees, task forces or commissions.

In addition to work on important problems not being studied sufficiently under the grant mechanism, the Institute now supports by contracts work on those problems that require large-scale cooperative efforts, collaboration of many research units and expert advice on design of experiments and evaluation of data. The latter include clinical trials in detection and management of hypertension; studies on the importance of risk factors in coronary heart disease; nationwide studies on blood lipids; intensive study of myocardial infarction in patients in special research units; and clinical trials of therapy for sickle cell disease. Contracts also finance special needs such as management of blood resources, development and testing of medical and surgical devices (including devices to assist or replace the failing heart and lungs), and provision for special surveys of research manpower needs.

The Council believes that the contract mechanism is essential for support of important research that would otherwise not be attempted. A careful balance must be struck, however, so that the future growth of the contract programs will not be at the expense of investigator-initiated, grant-supported research. The Council agrees that national planning *is* essential to mount a truly balanced program but believes that planning by a few highly competent individuals (either the permanent staff of the National Heart and Lung Institute or extramural scientists appointed to task forces or commissions) should supplement, but not replace, individual thinking by perhaps thousands. When the way ahead is not clear and a science base is lacking for a successful *directed* research effort, what is needed is an abundance of original ideas; these are most likely to come unpredictably from the imagination and intuition of individual scientists working in their laboratories, and less likely to come from administrators or their committees. There is a considerable risk for the future of the program in giving full authority for decisions about fruitful areas of scientific investigation to a relatively small group of either administrators or scientists. However, wise counsel at the national level can lead to acceleration of some important research programs when the needed research can be clearly predicted in orderly progression, and it can often lead to projects that secure valuable information difficult or impossible to obtain through the initiative of individuals.

For these reasons, the Council recommends that as the use of contracts for support of research increases:

- **This growth shall not be at the expense of the support of basic or mission-oriented research initiated by individual investigators;**
- **The areas of research to be supported by contract should be approved by the Council in advance;**
- **The scientific merit of research to be supported by contracts should be evaluated by consultant review groups before contracts are issued;**
- **Regular Council review should be required for contracts as well as for grants.**

The Council believes the contract should be considered a means for achieving a scientific goal rather than as an end in itself. To this end, it is recommended that the chief Federal officer responsible for contracts should be a member of the professional staff of the Institute and that the fiscal and legal administrators be advisory to him.

The Council also recommends that the National Heart and Lung Institute should make every effort to permit freedom in the conduct of contracted research if such freedom does not defeat the purpose of the contract.

For the contract mechanism to be truly effective, furthermore, it should provide greater stability of support than is now possible with an award limited to one year and the uncertainty of renewal year by year; the duration of the contract should be appropriate to the nature of the work. Evaluation of the contract program should be part of the annual review by the Council and its report to Congress.

VII. CONSTRUCTION

A lack of modern facilities for basic and applied research limits the advance of heart, blood vessel, lung and blood disease research in this country and, consequently, threatens the success of the National Program.

> **To mount a successful National Program against diseases of the heart, lungs and blood, the Council recommends that $60,000,000 be obligated for this purpose in FY 74 (thus enabling construction of research facilities to be started without delay) and $30,000,000 in each of FY 75 and FY 76.**

The basic sum in all years is for increasing the research capabilities of scientists working in existing programs of the National Heart and Lung Institute. The additional sum in FY 74 is to develop National Research and Demonstration Centers.

Because the results of research benefit the entire nation, recipient institutions should not be required to provide matching funds. National interests are best served by making construction funds available to those scientists and institutions that, given additional facilities, can make the greatest contibution to the National Program rather than to those whose scientific contribution may be less but whose institutions have non-Federal funds on hand to match Federal funds. The availability of complete Federal funding for construction would permit financially troubled schools to apply and to increase their research effort toward achieving national goals and would lessen redistribution of scientists from poor to rich schools.

> **Funds in a research grant may now be spent for alteration and renovation of existing research facilities. The present limit is $75,000 or 25 percent of the amount of the grant, whichever is less. The Council recommends increasing the upper limit to $250,000.**

VIII. BUDGET

1. FIVE YEAR BUDGET PROJECTION

The Council's projections for annual program budgets for the next five fiscal years (together with historical data from fiscal year 1972 and 1973) are presented in the Table on the following pages.

2. MULTIYEAR FUNDING

Tentative plans for any major new program, such as new Specialized Centers of Research or National Research and Demonstration Centers or new clinical trials, can be developed in advance, but requests for applications or proposals must await appropriation and allocation of funds. When these come late in a fiscal year, there is pressure on the National Heart and Lung Institute staff to complete and promptly announce plans to the community, and pressure on potential applicants to develop and submit proposals on short notice. This may limit applicants to a few institutions whose resources are already available and whose organization is already established, and exclude other institutions that might qualify, given more time to plan and organize. These problems are serious ones in that the excluded institutions might well develop the best programs. The problems can be avoided if the National Heart and Lung Institute is permitted to retain the funds intended for specific purposes beyond the fiscal year in which such funds are appropriated.

The need for more preparation time is particularly important for Center programs which require advice of extramural experts and consultations with the Council; a large commitment by the applicant institution of personnel, facilities and resources; interdepartmental cooperation and collaboration; and a good plan for internal management and administration. The need to retain funds is equally important in programs, such as clinical trials, that require a tool-up, phase-in time that may not be entirely predictable. Multiyear funding would also allow consultant review groups more time for objective evaluation and rating of proposals.

> **The Council recommends that funds for specifically identified programs should remain available to the National Heart and Lung Institute, for the purpose originally intended, until the end of the fiscal year subsequent to the one in which such funds were appropriated so that programs can be implemented on the basis of carefully developed plans, even though this may not be possible within the fiscal year of appropriation.**

3. NEEDS FOR STAFF AND FACILITIES, NATIONAL HEART AND LUNG INSTITUTE

The Council's recommendations for increasing many existing programs of the National Heart and Lung Institute and for creating new programs, as well as the

NATIONAL HEART AND LUNG INSTITUTE
FY 1972 (OBLIGATED): FY 1973 -- FY 1978
(DOLLARS IN THOUSANDS)

Program Activities	FY 1972 (obligated)	FY 1973 (estimated)	FY 1974 (estimated)	FY 1975 (estimated)	FY 1976 (estimated)	FY 1977 (estimated)	FY 1978 (estimated)
Research Projects and Program Projects	$102,835	$108,821	$141,113	$176,391	$220,488	$231,500	$243,100
Arteriosclerosis	(26,458)						
Cardiac Diseases	(22,106)						
Hypertension and Renal Diseases	(14,005)						
Pulmonary Diseases	(7,617)						
Thrombosis and Hemorrhagic Diseases	(12,117)						
Sickle Cell Disease	(5,581)	(8,000)	(9,500)				
Multidisciplinary	(14,951)						
Special Projects							
1. General Research Support Grants	8,325	8,149	---	---	---	---	---
2. Heart Cooperative Drug Study	3,514	4,900	4,900	500	---	---	---
3. Specialized Centers of Research	20,584	22,700	30,000	35,000	40,000	42,000	45,000
Arteriosclerosis	(9,515)						
Pulmonary	(6,467)						
Hypertension	(2,496)						
Thrombosis	(2,106)						
Other (see text)	---						
4. Control Programs*	---	---	5,000	15,000	30,000	31,800	33,700
5. Research Professor Grants	---	---	10,000	10,600	11,300	12,000	12,700
6. Young Scientist Education**	---	---	2,000	10,000	12,000	12,700	13,000
7. Professorial Group Grants	---	---	15,000	15,900	16,900	18,000	19,000
8. National Research and Demonstration Centers	---	---	24,000	36,000	48,000	51,000	54,000
9. Construction	---		60,000	30,000	30,000	0	0
Subtotal, Research Grants	135,258	144,570	292,013	329,391	408,688	399,000	420,500
Fellowships and Training Grants:	24,905	22,000	17,139	12,000	6,000	---	---
Laboratory and clinical research	18,259	18,741	20,376	22,000	24,000	25,400	27,000

R&D Contracts:							
Heart and vascular:							
Myocardial Infarction (MIRU, SDS, and anti-arrhythmic drugs)	8,027	9,980	10,500	13,000	14,000		
Lipid metabolism	5,485	8,378	10,400	11,000	11,700		
Hypertension clinical trials	3,971	6,100	7,400	8,500	9,000		
Heart cooperative drug study	424	450	500	---	---		
Multi-risk factor trials	3,268	7,240	10,000	12,000	12,000		
Education programs-hypertension*	---	---	2,000	3,000	4,000		
Other clinical applications	1,108	1,307	750	1,000	5,000		
Subtotal, Heart and vascular	22,283	33,455	41,550	48,500	55,700	59,000	62,600
Respiratory diseases	1,585	2,330	2,885	8,000	10,000	10,600	11,200
Technological applications	10,572	9,600	12,500	14,000	15,000	15,900	16,900
Blood diseases and resources:							
National blood resources	5,504	5,500	8,000	12,000	15,000		
Thrombosis clinical trials	---	---	5,000	5,000	6,000		
Sickle cell: research	2,326	3,500	3,700	4,000	4,500		
clinics, HSMHA*	1,975	2,000	3,800	4,000	3,000	2,000	1,000
Subtotal, Blood diseases and resources	9,805	11,000	20,500	25,000	28,500	29,000	29,700
Other:							
National plan	---	1,000	600	1,000	1,000		
Miscellaneous	354	884	892	1,000	1,000		
Animal models	---	---	1,900	2,000	3,000		
Subtotal, Other	354	1,884	3,392	4,000	5,000	5,300	5,600
Total, R&D Contracts	44,599	58,269	80,827	99,500	114,200	119,800	126,000
Biometry and Epidemiology	1,536	1,700	1,791	1,900	2,000	2,100	2,300
Research Management & Program Services***	8,016	10,000	10,000	12,000	14,000	15,000	16,000
Total	232,573	255,280	422,146	476,791	568,888	561,300	591,800

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*Planned under the authority of Section 414 of the Act.

**In the event these funds are not made available, Council recommends the addition of 1.5 times the amounts shown on this line to the amounts for research grants.

***Includes the Office of the Director of the Institute and the scientific administration of grants and contracts.

added responsibilities authorized by the National Heart, Blood Vessel, Lung, and Blood Act of 1972, cannot be carried out without a considerable increase in budget and space for the Institute's Research Management and Program Services. There is urgent need for additional, highly qualified *professional* staff and expert consultants to maintain a high level of competence for program planning and evaluation, for critical scientific analysis of programs, for identification of both neglected and overworked areas, and for coordination of national efforts directed toward early diagnosis, treatment and prevention of heart, blood vessel, lung and blood diseases.

Because the present professional staff of the National Heart and Lung Institute is greatly overextended, the increment in professional staff must be greater than that required simply for new program management if maximum advantage is to be gained from appropriated funds. An indication of the magnitude of the staffing problem is that in the last decade, from 1963 to 1973, the obligations of the National Heart and Lung Institute have increased by 93 percent (from $120 million to $232 million) while the total staff of the Institute has actually *decreased* by 1.3 percent (from 673 to 664).

Several immediate needs present themselves. New responsibilities have been added for lung diseases, blood diseases including sickle cell disease, control programs and the establishment of National Research and Demonstration Centers. Other new demands are created by the expanded activities of the Council and the U.S.-U.S.S.R. Cooperative Health Agreement. Immediate increase in staff is required in each of these areas.

The Council's National Program recommends expenditure increase from $255,280,000 in FY 73 to $422,146,000 in FY 74, an increase of 65 percent. If this budget recommendation is followed, the staff responsible for all extramural programs will have to be increased appropriately to plan and oversee the increase in expenditures. The detailed justification of specific positions will have to be prepared by the Institute. The Council confirms that under-administration can be as wasteful as over-administration.

Similarly the Council calls for an increase in expenditures of 45 percent between 1974 and 1978. An increase in staff certainly will be required to handle this responsibility.

IX. NATIONAL PROGRAM REVIEW AND EVALUATION

ANNUAL REVIEW OF PROGRAMS AND PRIORITIES

The Council is required by the Act to submit a report to the Congress in January of each year on the progress of the National Program toward its objectives. The Council is also required to assist the Director of the National Heart and Lung Institute in preparing an annual report on the five-year plan with annual extensions of the plan. The Council holds these functions to be very important for the success of the plan because the National Program must be flexible and must respond to scientific opportunities and exploit new leads. Therefore, it has set up a schedule for overall review of each of the major programs on which it advises.

- In September of each year, research grant, program project, Specialized Center for Research, contract and other programs will be reviewed with the Director and staff of the National Heart and Lung Institute. Prior to the September Council meeting, hearings may be conducted to reevaluate priorities in each disease area. This will give the Council opportunity to respond to national needs and to take advantage of recent scientific advances. The Council will suggest changes, deletions and new emphases in the National Program priority recommendations.

After the Council discussion at the September meeting, the required report will be written by a subcommittee according to an approved format. Further Council review will be in November or December at which time the report will be forwarded, together with budget, staff and legislative recommendations, to the President and Congress.

In developing its report, the Council will pay particular attention to the effect on the National Program of the provisions of Section 419B of the Act which allocate 15 percent of the National Heart and Lung Institute appropriations to the lung and blood fields respectively.

> **The Council believes that the experts or consultants authorized by Section 413 (c)(1) of the Act could provide in-depth analysis of the various programs for use in program evaluation, both by the Institute and the Council.**
>
> **Periodic review every few years by an ad hoc group, separate from the Council, should be considered. Such a group would analyze the Program and recommend improvements in its operations.**

PEER REVIEW OF PROPOSALS FOR GRANTS, CENTERS AND CONTRACTS

The system of peer review of research proposals by knowledgeable experts, followed by review by the

Councils, has been one of the most successful undertakings of the National Institutes of Health, and has assured high quality and productivity of the total research effort.

> **The Council strongly advises that the peer review system, including Council review, should be extended to all parts of the program of the National Heart and Lung Institute.**

The Council believes that the peer review system has been as effective for program projects and specialized centers of research as it has been for individual research grants. Before awards are made for National Research and Demonstration Centers for heart, blood vessel, lung and blood diseases, it is important that the same careful review of all scientific proposals be carried out by appropriate experts just as for other types of research effort. The Council believes that, because of the size of these Centers, multiple peer review mechanisms will need to be utilized, including site visits, special and ad hoc review groups, and, when needed for certain individual projects within the Center, referral to study sections.

The Council believes that peer review of contract awards should be as similar as possible to review of research grants. This would entail review by the Council of individual proposals and recommendations of initial review groups.

A special section within the Institute, separate from the ongoing program branches, should be responsible for appointments to peer review groups of the National Heart and Lung Institute.

To assure adequate Council review of proposals in all areas—heart, blood vessel, lung and blood diseases—balance must be maintained in the areas of expertise represented by the scientific members of the Council.

Appendix B

Summary of Surveys of Manpower Needs

Appendix B

Summary of Surveys of Manpower Needs

- A Nationwide Survey in Cardiology Training and Manpower Requirements is being conducted through a contract with the American College of Cardiology. The goal of this survey includes a characterization of the practice of cardiology and a determination of the manpower resources presently available, the expertise needed, and the training which is requisite. The final report from this project has been completed.

- A Manpower Survey in Thoracic Surgery was conducted through a contract with the Manpower Executive Committee of the American Association for Thoracic Surgery-Society of Thoracic Surgeons. The report from this project, which was completed in the fall of 1973, includes a classification of the current manpower in thoracic surgery in nine census regions of the United States and the provision of data on the geographic location, work load, age, and distribution of these surgeons in relation to the population density in various parts of the United States.

- A Survey of Professional Manpower in Pulmonary Diseases was prepared for the National Heart and Lung Institute by a joint committee of the American Thoracic Society and American College of Chest Physicians in collaboration with the Subspecialty Board on Pulmonary Diseases of the American Board of Internal Medicine. This report was issued in November 1972 as a service to the biomedical community. (The report may be obtained from the Division of Lung Diseases, National Heart and Lung Institute, Building 31, Room 5A10, 9000 Rockville Pike, Bethesda, Maryland 20014.) The report pointed out glaring insufficiencies in current manpower management in pulmonary research. The report concluded that "of 105 U. S. medical schools, 14 have only two full-time equivalent faculty involved in pulmonary graduate and undergraduate training and research. There are 131 full-time and part-time funded pulmonary faculty vacancies and an additional 292 are needed within the next two years."

- The Division of Blood Diseases and Resources is currently preparing a proposal for manpower development in research hematology. This proposal is designed in conformance to the emerging guidelines for postdoctoral education being formulated by the Department of Health, Education, and Welfare. In essence, the aims of the proposal include an identification of areas of hematology in which a significant research effort is lacking, a quantification of the need for researchers in each area, and an outline of a plan for manpower management in this area of research. Representatives of the National Institute of Arthritis, Metabolism, and Digestive Diseases have extended their cooperation in this endeavor, and opinions from the non-federal community of academic hematologists have been solicited. The proposal will also take into account the Survey of Staff Positions in Academic Hematology in 1971 (*Blood* 40:574-584, 1972).

Appendix C

Training Recommendations of the President's Science Advisory Committee

Appendix C

Training Recommendations of the President's Science Advisory Committee

Research Training Programs, Research Fellowships, and Research Career Development Awards

At least four types of support for graduate education presently exists: training grants, national fellowships, research grants by way of employment of graduate students and research assistants, and university fellowships or assistantships.

Training Programs—Grants for training programs provide funds for stipends and tuition to the student and, in addition, funds for salaries of faculty, equipment, and supplies. They are made to the staff of a department and are specifically designed to support training in research. *Training grants have become a major source of support of basic science departments.* The external review provided by the project site visit and the review by the committee evaluating the applications for a training grant have provided national standards for graduate training.

The training grant is also a major source of support in the clinical departments of the academic medical center. Here it supports chiefly post-doctoral fellows who will become the physician-scientists of the future. In other instances it supports the training of clinical specialists in areas of manpower scarcity, such as neurology and psychiatry. The training grant has been an important vehicle in developing research and new clinical competence in specialized clinical areas such as endocrinology, for example. In addition to spending the predominant amount of their time in research training, the endocrinology trainees also serve as consultants in connection with patients with complex clinical problems involving the endocrine system. To develop competence as clinical endocrinologists and to obtain patients for their studies, these trainees operate special endocrine clinics (such as a Diabetes, Thyroid, or Kidney Stone Clinic) under faculty direction, and thus indirectly provide a large amount of patient care and service. One or more of the involved faculty members is supported in part with salary money derived from the training grant in proportion to the amount of time devoted to supervision of research training. The grant also provides some money for supplies and equipment for the use of trainees. In many instances, studies conducted by the trainees also provide highly specialized diagnostic procedures for which patients with complicated endocrinological problems are commonly referred to academic medical centers. Such services cannot be provided by the financing of Medicare and Medicaid because *these programs have no capacity to create the expert capabilities required to render complex services.*

Research Fellowships—An application for a training grant program is made by the institution. Application for a research fellowship is made by an individual who has been accepted for training by a department of an institution. Predoctoral fellowships are available to graduate students in basic science departments but not to candidates for dental, medical, or veterinary degrees. Postdoctoral research fellowships are made available to Ph.D.'s and M.D.'s for advanced research training. These fellowships may be supplementary to research training programs in instances in which departments can train more men than can be funded from the training grant itself. They also support men in advanced training in departments in which a training grant may not exist, or even in government agencies including the National Institutes of Health in circumstances in which intramural funds are not available.

The fellowship program of NIH expanded less rapidly than the training grant programs. The annual number of fellows grew to a little more than 1,000 in fiscal 1962, and remained at under 2,000 through fiscal year 1967. Recently NIH decided to terminate its predoctoral fellowship program. This act and the cutbacks by NASA, AEC, and NSF raised the question for prospective students whether or not science really has a high priority in this country and whether they should pursue it as a profession. The cutback in the fellowship program is particularly difficult for those departments that do not have grants for training programs and it is virtually disastrous at a time when training programs and research grants are being curtailed. This problem is dealt with further under "Effects of Termination of Training Support."

Research Career Development Awards—An institution may apply for salary support for a young faculty member who has demonstrated unusual competence and promise in research and who needs a number of additional years for maximal development of his research creativity and potential. Such an award enables him to devote nearly all of his time to research and research training under guidance of a more senior faculty sponsor, while also engaging in teaching and, in the case of an M.D., in a limited amount of clinical work so as to maintain and develop his full range of medical skills.

Various combinations of support from training grants, direct fellowships, and research career development awards, have provided substantial stability and flexibility in the development of highly competent young investigators in both pre-clinical and clinical sciences. These men have provided an uncommon source of faculty strength within the medical school at a time when the fruits of the biomedical science effort are beginning to have a substantial influence upon the understanding of disease and the scientific base of medical education.

Some Estimates of Future Needs of Biomedical Scientists and Teachers—Bioscience graduates provide research workers for universities, colleges, institutes, agency laboratories, and industry. They also provide teaching faculty for colleges, universities and medical school departments. The exact number of Ph.D.'s in biomedical sciences needed in research and teaching during the next twenty years is not known. If research grant monies are to remain at a plateau it may not be desirable to train an ever-increasing number of Ph.D.'s to conduct biomedical research in universities and colleges, but the need for scientists as research workers in agency laboratories, institutes and, in particular, industry, is not likely to diminish. The implication that we are training a surplus of biomedical Ph.D.'s appears unfounded, at least to the panel. All but 1.3 percent of these Ph.D.'s graduating in 1968 and 1969 found positions in which they are appropriately utilizing their graduate education, although not all of them have found the type of position to which they originally aspired. Information regarding the fate of biomedical Ph.D.'s graduating in 1970 will not be available until early in 1971.

In 1967 and again in 1968, the Medical Scientist Training Committee of the National Institute of General Medical Sciences (NIGMS) made estimates of current and future faculty needs of medical schools taking into consideration the turnover of faculty by retirement, the probable increase of numbers of medical students and house officers in existing schools, and the establishment of new medical schools as projected through 1985. These estimates called for the production of 1,000 to 2,000 new faculty members per year for the next ten to twenty years. It was projected that about one-third of these would need to be specially trained as research scientists in basic and clinical sciences and that, in addition, perhaps 20 percent of the M.D. faculty members would require substantial dual training in a basic science discipline. (These figures do not include the requirements of Ph.D. scientists who will find places outside of the academic medical centers in both basic research and mission-oriented research and development.) A shortage of faculty causes inflation; witness the "market price" of academic anesthesiologists and radiologists compared with faculty in other clinical departments. Figure 3 shows the budgeted unfilled faculty positions in American medical schools, year by year through 1969.

Effects of Termination of Training Support and Fellowship Program—During the past five years, training support from NIGMS and the categorical institutes has leveled off. In addition, fellowship support from other sources, such as NSF, AEC, and NASA, has decreased. The loss of a training grant can have a serious impact on a department, far beyond the reduction in output of Ph.D. scientists or physician scientists. In both preclinical and clinical departments the training grant provides not only stipends for post-doctoral trainees, but also salaries for faculty and money for supplies and equipment involved in training. In addition, a research training program in a clinical department provides expertise for student and house staff training and manpower for the operation of the specialty clinics in which a large amount of clinical care as well as training takes place.

There are now no alternative sources of support that can be utilized to replace the training grant or fellowship or Research Career Development Award. Strong basic science departments and clinical units can disintegrate in a short time when training grants and fellowships are withdrawn. It is an illusion to believe that the funds for training and fellowships can be siphoned from research grants. At present, research grants are being used to support graduate assistants at nearly their full capacity. Furthermore, research grants are also being curtailed and are being forced to absorb the increased cost of operation resulting from inflation.

John Walsh states in Science (Volume 168, 1970, p. 1561) "It should be possible with better planning to minimize damage done in a period of budget contraction but, unless policy makers come squarely to grips with problems posed by cuts such as those in graduate support, they are likely to find themselves locking the lab door after the researchers are gone."

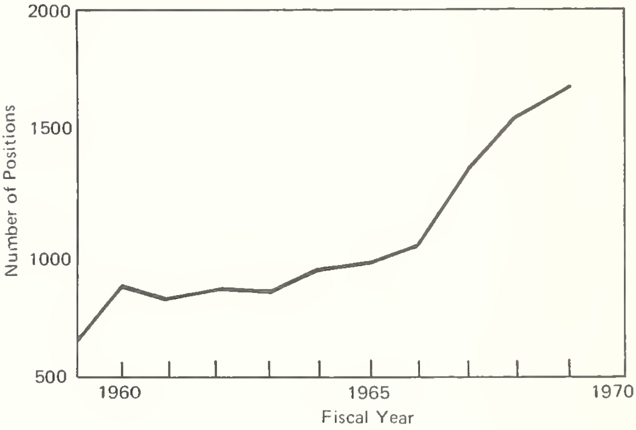
The impact of fellowship curtailments in the clinical departments affects not only research, but also the care of patients. Many patients who are the beneficiaries of the highly specialized services rendered by trainees are medically indigent or near-indigent, and only a fraction of them are covered by Medicaid and Medicare programs. Hospitals are already incurring large deficits from the care of such patients due to the low level of reimbursement for services provided. Clearly, additional charges to patients will not substitute for training grants either. There is no alternative source of support and withdrawal of training funds can only result in the loss of academic and clinical expertise in the medical centers and curtailment of highly specialized diagnostic services to patients. These disruptions will affect the very institutions that provide the most complicated and highly specialized care to patients who have been referred to them for such care because of the lack of appropriate facilities and expertise in the local community.

About 40 percent of the acute care beds and 80 percent of the residents in specialty training in this country are found in academic medical centers and their affiliated hospitals.

FIGURE 3

BUDGETED UNFILLED MEDICAL SCHOOL FACULTY POSITIONS

(Source: Association of American Medical Colleges)



Appendix D

Program Announcement and Guidelines for National Research and Demonstration Centers

Appendix D

Program Announcement and Guidelines for National Research and Demonstration Centers *

INTRODUCTION

The National Heart and Lung Institute (NHLI) announces its intent to establish a limited number of National Research and Demonstration Centers as authorized in the National Heart, Blood Vessel, Lung and Blood Act of 1972 (P.L. 92-423).

A National Research and Demonstration Center is envisioned as a national resource attached to a major medical complex and dedicated to working in close collaboration with the NHLI to further the goals of the National Heart, Blood Vessel, Lung and Blood Program through a multidisciplined, coordinated, yet flexible, approach to research, education (public and professional) and demonstration of the applicability of the results of research. It is the inclusion of education and demonstrations and the coordination of these programs with research and training efforts that sets a National Research and Demonstration Center apart from other types of programs.

Awards will be based on national competition. Only a limited number of awards will be made at the start of the program; additional Centers may be established as experience is gained. Although the financial plan for the NHLI for fiscal year 1974 provides for National Research and Demonstration Centers, the ability of the Institute to make any awards for Centers in fiscal year 1974 is contingent upon the availability of appropriated funds.

THE NATIONAL HEART, BLOOD VESSEL, LUNG AND BLOOD PROGRAM

The Act authorizes the Director of the NHLI, with the advice of the National Heart and Lung Advisory Council, to develop a plan for a National Heart, Blood Vessel, Lung and Blood Program which will expand, intensify and coordinate activities in an accelerated attack on heart, blood vessel, lung and blood problems. The overall goals of the National Program are: To promote health, to prevent diseases, to treat disease and to restore health.

The plan for implementation of the National Program identifies three major categories of actions, all linked one to the other: (1) actions that can be applied now for the better prevention, detection and treatment of disease; (2) actions that draw upon existing information, but require further testing and evaluation before they can be properly applied; (3) actions that require acquisition of new and basic information because the current state of knowledge is incomplete.

---

* National Heart and Lung Institute bulletin, August 20, 1973.

The following list includes major areas of interest to the Divisions of the NHLI primarily involved in the Centers program. The list is neither all inclusive nor exclusive, nor is it necessarily in an order of priority of interest.

Heart and Blood Vessel Diseases: atherosclerosis, hypertension, coronary heart disease, arrhythmias, heart failure and shock, cerebrovascular disease, peripheral vascular disease, congenital and rheumatic heart disease, cardiomyopathy and infections of the heart and technological applications and devices related to the heart and vascular disease.

Lung Diseases: structure and function of the lung, emphysema and chronic bronchitis, fibrotic and immunologic lung diseases, pediatric pulmonary diseases, respiratory failure and technological applications and devices related to lung disease. Cancer of the lung, upper respiratory infections and tuberculosis are covered by other programs of the National Institutes of Health (NIH) and therefore they are not included as major problem areas for the NHLI.

Blood Diseases and Blood Resources: for blood diseases, the hemophilias, thromboembolic disorders, platelet abnormalities, mircrocirculatory thrombosis, thromboembolism in relation to prosthetic devices, sickle cell disease and related disorders of the red blood cell; for blood resources, a nationwide blood system, blood therapy and transplantation biology.

REQUIREMENTS FOR A NATIONAL RESEARCH AND DEMONSTRATION CENTER

Role

National Research and Demonstration Centers can play an important role in achievement of the goals of the National Program by bridging the gulf between fundamental research and application of the results in health care and the prevention of disease. The presence in a Center of scientists and other professional personnel representing many disciplines can create an environment in which participants interact in an efficient and productive way. In particular, the interaction between scientists and practitioners of various medical specialties should speed the solution of categorical disease problems related to the mission of the NHLI. Such a setting also can create an ideal environment for training future biomedical scientists.

Program of a Center

A National Research and Demonstration Center is envisioned as broad in scope, encompassing a wide range of activities in a continuous spectrum from fundamental research to education (public and professional) and demonstrations of innovations in health care delivery and community services. A Center is not intended to be a direct service facility for the local community nor a means of funding primary health care.

Each applicant organization will be expected to propose its own program based on local interests and resources. Preferably, the proposed Center program should focus on one of the major areas of the National Program -- heart and blood vessel diseases, lung diseases, blood diseases, or blood resources. However, the Center may address any combination of these areas if the resultant combination can be shown to be related directly to the primary emphasis of the Center and to meet more effectively the goals of the National Program.

The proposed program must include each of the following components:

1. A fundamental research program, in a field related to the main thrust of the Center.

2. A clinical research and clinical application program. Each Center should plan for demonstrations of the applicability, in a community setting, of diagnostic, therapeutic or preventive measures. Inasmuch as the ultimate goal is prevention through solution of disease problems, Center staff should have access to clinical facilities where sophisticated clinical investigation can be conducted.

3. An environment conducive to the training of young scientists. NHLI cannot provide direct stipendiary support for trainees, but the Institute can support salaries for services rendered to the Center program, and can support activities and resources which may provide a stimulating environment for training.

4. An information and education program. Each Center should be a focus for continuing education for professional and other health personnel and a source of information for the community.

A key attribute of a Center should be the ability to translate, rapidly and effectively, appropriate results of research into health care and to demonstrate applicability in such a way that the particular activity can become standard practice not only in the community in which it is demonstrated, but in other communities as well. Each demonstration project should be limited in time and scope. Once effectiveness has been shown, support for the given activity should be derived from community resources and no longer from NHLI support for the Center. Center programs should be sufficiently flexible to allow initiation of new demonstration projects as and when dictated by advances in research.

An equally important aspect of a Center program should be public and professional education. The aims should be to alert the public to the possibilities for prevention and control of disease and to increase the awareness of physicians and allied health personnel of specific disease problems. It is not the intent to use Center support for education of medical students or house staff.

The Center may include other activities, such as prevention and detection or intervention programs, emergency medical services, or programs related to local interests and resources, as long as the emphasis remains on research, education and demonstration.

Responsibilities of Applicant Organization

A National Research and Demonstration Center should be an identifiable, organizational unit in a major medical complex. The applicant organization will be expected to have the personnel, facilities and resources necessary to initiate the program and to make a commitment of these staff, facilities, and resources to the Center. The needs and the support required to bring the program to full strength, particularly for the demonstration and education aspects of the program, should be projected in the application for support. It is not the intent to establish Centers *de novo* nor to use Center support as a means of creating a cardiovascular, lung or blood capability in an institution where it does not already exist.

Participating staff in key positions should be willing to make a reasonable and long-term commitment to the Center. The Director should be an experienced and respected individual, and one who can provide leadership for the total program.

The applicant institution should be prepared to provide the space necessary for the Center as proposed. While P.L. 92-423 authorizes funds for construction of new facilities, the availability of such funds is uncertain at the present time. If construction funds for National Research and Demonstration Centers become available in the future, additional guidelines will be issued and separate applications invited for construction. Funds for limited alteration and renovation of existing space, up to a total of $250,000, will be available and may be requested.

Collaboration with National Heart and Lung Institute

While each Center will be expected to develop its own program in accordance with local talents, interests and resources, each Center must be responsive to the National Program and must be willing to work cooperatively with the NHLI in furthering the goals of the Program. To facilitate coordination between the Center and the Institute, the Institute will designate one or more members of its staff as program officer(s) to work closely with the staff of the Center on scientific, fiscal and administrative matters. The program officer(s) will be in a position to coordinate plans for any special projects of mutual interest to the Institute and the Center or perhaps to several Centers. The Program officer(s) will make regular visits to the Center and will be responsible for evaluating progress and reporting to the Institute.

MECHANISM OF SUPPORT

Centers will be funded by the grant mechanism, but as noted above, under conditions that will require close coordination with the NHLI. Support for a Center may be derived entirely from the Center grant or may be derived in part from other sources -- Federal, local, public or private. The applicant organization undoubtedly will support some Center activities with its own funds as part of its commitment to the Center. Financial assistance from the community might be helpful for the development of demonstration projects that will be time-limited and will require community support once the demonstration phase is complete. A Center may serve to attract and coordinate activities related to common interests.

When multiple sources of support are used, other sources should not be so large or critical as to determine the direction of the Center program. Furthermore, care must be exercised to avoid duplication of funding for the same activity. Regardless of source of funds, the Center Director should be able to exercise control over the entire program, in a manner consistent with good management principles.

OTHER NATIONAL HEART AND LUNG INSTITUTE PROGRAMS

The NHLI now supports research programs, some multidisciplinary and multicategorical, by a variety of mechanisms and will continue to do so. A National Research and Demonstration Center is intended to be more comprehensive and therefore not a subsititute for any of the following, although any or all may become a component part of a Center.

Program Projects. The grants provide support for a group of investigators who wish to bring their various talents to bear on related aspects of research on cardiovascular, pulmonary, or blood diseases, or blood resources. The program usually has a clearly defined focus. It may be interdepartmental or intradepartmental, basic and/or clinical, and the grant may support either core resources that are shared or the research needs of the participating investigators, or both.

Specialized Centers of Research (SCOR). The essential characteristic of a SCOR is an attack upon problems which relate to prevention, diagnosis and treatment of specific diseases. The areas in which SCORs are established are identified by the NHLI, and the program of a SCOR must be dedicated to one of these areas, with major emphasis on one or more of the identified problems in the area. The program may include basic, applied or developmental projects, and often includes clinical investigation. The emphasis is on research. What differentiates a SCOR from a Program Project is the close coordination of the SCOR program by the NHLI staff. At present time, the Institute funds SCORs in arteriosclerosis, pulmonary diseases, thrombosis and hypertension. Additional SCORs may be established in other areas to meet programmatic needs.

Mission-oriented Research. This includes research and development, usually supported by contract, in areas in which specific targets are identified by the NHLI, and/or the nature of the research requires collaboration with the Institute. The areas thus covered may include certain topics in fundamental and clinical research, but are more likely to be related to clinical applications, clinical trials of therapy and technological developments.

Prevention and Control Programs. In addition, National Research and Demonstration Centers are not intended to substitute for the Prevention and Control Programs authorized by the Act. These will be established independently and will be primarily education programs directed to the practicing medical profession and to the public. The National Program includes plans for Prevention and Control Programs in each of the major disease categories of importance to the Institute.

In summary, a National Research and Demonstration Center is envisioned as being broader in scope than any of the above, encompassing a wide range of activities in a continuous spectrum from fundamental research to education (public and professional), and demonstrations of health care delivery and community services. It is the inclusion of education and demonstration programs and the coordination of these programs with research and training efforts that sets a National Research and Demonstration Center apart from other types of programs.

REVIEW CRITERIA

The NHLI invites the submission of applications for support of National Research and Demonstration Centers. The proposals will be evaluated in national competition with each other. Primary review will be by a technical review group of consultants and may involve a site visit. Secondary review will be by the National Heart and Lung Advisory Council. Major factors to be considered in evaluation of proposals will include:

1. The strength and scientific excellence of the overall program and the technical merit of the proposed program components.

2. The significance of the program in relation to the Center's goals and the goals of the National Program.

3. The competence of the senior personnel in their respective fields and their ability to carry out their assigned roles.

4. The resources for a program of information and continuing education for the health profession and the public.

5. Access to the Community in relation to demonstration projects.

6. The intellectual and physical environment for training young scientists.

7. The arrangements for (a) day-by-day management; (b) internal quality control of on-going research, training, and demonstration programs; (c) continuity of the program; (d) allocation of funds and fiscal responsibility in handling awarded funds.

8. The requested budget in relation to the proposed Center program.

9. Integration of the multidisciplinary effort within the Center and coordination of the research effort with demonstration and education activities.

10. Willingness to establish an effective partnership with the NHLI.

PROGRAM EVALUATION

The Act requires the Director of the NHLI to prepare an annual report on activities, accomplishments and progress under the National Program. In developing these reports, the Institute plans periodically to evaluate the Centers program. Areas to be assessed, in addition to scientific and technical merit and advances, will include the effectiveness of the Centers in furthering the goals of the National Program, the effect of the Centers on their respective sponsoring institutions, the increase in professional and public awareness of heart, lung and blood problems as a result of Center activities, and the improvement in the standard of practice (locally and elsewhere) as a result of Center-sponsored demonstations.

METHOD FOR APPLYING

A. Meeting of Potential Applicants

The Institute plans to hold a meeting of representatives from interested institutions prior to submission of proposals. Such a meeting is tentatively scheduled for October 2, 1973 in the Washington, D. C. area. The purpose is to describe the National Research and Demonstration Centers program in more detail than is possible in this Announcement and to enable potential applicants to ask questions. To assist us in making plans for the meeting, we would like to know the names of the individuals who are interested in attending. The reply form enclosed for this purpose should be returned as promptly as possible. We will send additional information about the arrangements directly to those planning to attend.

B. Letter of Intent

Prospective applicants should submit a letter of intent to the NHLI not later than November 1, 1973. The Institute requests such letters only to have some idea of the number of applications that may be expected and to start planning for their review. A letter of intent is not binding and will not enter into the review of any proposal subsequently submitted.

The letter should be limited to 1 or 2 pages. It should briefly describe the Center's emphasis, touch upon the main research studies and the principal demonstration programs to be proposed, mention the key participants, and give a rough estimate of the level of support required, in direct costs. Inquiries about the National Research and Demonstration Center program should be addressed to:

Jerome G. Green, M.D.
Director, Division of Extramural Affairs
National Heart and Lung Institute
National Institutes of Health
Bethesda, Maryland 20014

C. Format for Applications

Proposals for National Research and Demonstration Centers should be submitted on Form NIH-398, the application form for the traditional research project grant. The format for presentation of a National Center proposal should be as outlined below. The completed application should be returned to the Division of Research Grants, NIH, but it should be clearly identified as a proposal for a National Research and Demonstration Center related to the National Heart, Blood Vessel, Lung and Blood Program. At the same time as the application is mailed, a letter should be sent to Jerome G. Green, M.D., Director, Division of Extramural Affairs, National Heart and Lung Institute, NIH, advising that a proposal for a Center has been submitted to DRG.

1. Title page

Complete this in the same manner as for a research grant proposal.

2. Objectives

Page 2 of the application form, although entitled Research Objectives, is meant to furnish a very brief key to the total proposal for use by the Science Information Exchange and by NIH and NHLI for program analysis. Therefore, it should include the research, training and demonstration components of the program. The text should not exceed the allotted space. Only key professional personnel need be listed at the top of the page.

3. Table of Contents

This should afford a quick reference to the various sections of the application such as individual projects, specified budgets, organization and administration, etc.

4. Introductory Summary

This should be a short but substantive outline of the proposed Center program. In addition to a general overview, the summary should include mention of facilities, personnel, administrative and organizational structure and availability of subjects. Access to community health services, collaborative efforts involving community resources and any additional points relevant to the program should be noted.

5. Individual Program Components

Each proposed activity, component or core facility should be described separately and in sufficient detail for experts to assess its technical merit, and should be accompanied by the requested budget. Activities that will be part of the Center but do not require funding from a Center grant should be included, but the description may be brief. Each segment of the program should be justified in terms of relevance to the National Program.

For research components, state the hypotheses on which the specific projects are based, their relevance to the goals of the Center, and how their progress will affect other Center activities. Indicate the mechanism that will be used to translate relevant research accomplishments into practical application. For clinical investigations, include the criteria for selection of patients as well as the number to be studied annually.

For demonstration projects or prevention and control programs, state the objectives and indicate the relevance of the effort to the goals of the Center and the National

Program, as well as the effects upon other Center activities. Include the criteria for selection of populations or subjects. Specify how progress will be monitored and effectiveness of the program evaluated. The probability of reducing the methods and techniques to standard practice and transferring the results to other communities should be indicated. Plans should be included for phasing out support for these programs, and phasing in support from some other source when the objectives have been achieved.

The following format is suggested for individual components:

Title.

Responsible Individual and other key participants.

Specific Aim including hypotheses to be tested, if any.

Method of Procedure, presented in sufficient detail to permit evaluation, but not in minute detail if the techniques are widely accepted. Techniques that are new or different should be explained, preferably in an Appendix.

Significance to the goals of the Center and the goals of the National Program, indicating how the results obtained will be integrated with those of other program components.

Previous Work by the responsible persons in the same or related fields.

Previous Work by Others, in summary form, including relevant references.

Present Support for this activity.

6. Training Environment

Describe the training environment and opportunities, keeping in mind that direct Federal support for stipends will not be available. State whether any formal training programs are anticipated (other than intern and residency programs). Outline plans for any such programs, indicating whether the training will be for professionals to engage in research or clinical medicine, or for allied health professions personnel.

Facilities

Describe facilities available to the Center, including facilities of the applicant institution and other institutions collaborating in the program.

Describe new facilities necessary for the program and state how they will be obtained. Federal funds to support construction for a Center are not available at the present time. However, alteration of exisiting space is permitted and funds may be requested for this purpose up to a maximum of $250,000. Include line drawings to demonstrate feasibility, adequacy and relationship to other relevant facilities.

Describe the geographic distribution of space and personnel, and plans for coordination of effort in central and outlying facilities. Geographic proximity is desirable but not mandatory, and obviously not always possible for demonstration activities.

Describe any centralized or core facilities to be shared by participants.

8. Patient and Subject Availability

Outline, and document if possible, the availability of patients and subjects for the various components of the Center program. This is particularly important for demonstration, prevention and control programs that may require cooperation with community physicians and collaboration with existent community health programs.

9. Organization and Administration

Describe the administrative relationships of the proposed Center within the sponsoring institution:

- Where administrative responsibility would reside
- To whom the Director of the Center would be responsible
- Relationship of the Center with other components or centers within the institution
- Arrangements for appointing a new Center Director should the need arise

Describe the organizational framework within the Center, naming responsible individuals if possible.

Describe lines of responsiblity within the Center for:

- Administrative and fiscal matters
- Planning and conduct of research
- Clinical matters
- Training programs
- Demonstration programs
- Information and education programs
- Integrating the various programs
- Data storage, retrieval, and analysis

Describe plans for monitoring performance in the program, indicating how decisions will be made regarding phasing out of completed or unproductive components, initiation of new components or changes in direction of on-going work. If an in-house executive committee is contemplated, outline its composition. If an outside advisory committee of consultants is planned, indicate the categories of individuals who would be invited to serve.

Describe plans for determining when demonstration programs have achieved their goals.

10. Other Support.

List all active, pending or planned support of the major participants indicating which support is related to Center activity. It is not necessary, or even desirable, that the Center grant be the sole source for all Center activities. Support from two or more sources may be applied toward various aspects of a given project, but duplication of support for the same activity is not allowed. Indicate how the multiple sources of support would be interrelated and/or what support might be relinquished in favor of a Center grant.

11. Budget

The budget should be presented as follows, using the budget categories listed below:

- Detailed composite budget for all support requested for the first year, placed at the beginning of the application, before the textual description of the Center proposal.

- Summary budget, by major category only, for each year of requested support, entered on the preprinted page in the application form and placed immediately after the composite budget. The Act limits each project period to five years, therefore no more than five years should be requested.

- Detailed budget for the first year of each proposed Center component, placed in the application just before the text of the relevant section.

Budget categories:

A. Personnel - list professional and non-professional personnel using the format on page 3, Form NIH 398

B. Consultants

C. Equipment - (a) purchase; (b) rental

D. Supplies

E. Hospitalization costs

F. Outpatient costs

A Center is not intended to be a facility for health care delivery. Only those patient care costs that are directly related to the various research, training, or demonstration components of the Center program may be charged to the grant. The rates applied should be those negotiated with the institution by the DHEW Division of of Cost Policy and Negotiation.

G. Travel (domestic only)

H. Alteration and renovation

Funds may be requested for this purpose up to a maximum of $250,000 during the entire project period.

Funds for construction of new facilities are not available at the present time. Should such funds become available in the future, awards will be based on separate applications reviewed in a separate competition.

I. Publication costs

J. Other direct costs - (a) Purchased services or contracts, (b) Other

The budget for any program activity that will be carried out in another institution, but will be supported by contract from the applicant organization, should be entered in this category, either as "contracts" or "purchased services". This may include demonstration projects in affiliated hospitals. The budget for such activity should be itemized and should include applicable indirect costs. None of the expenses of an activity to be supported by contract should be charged to any other major category. Please contact NHLI staff for detailed information, particularly in regard to support for a consortium.

12. Biographical Sketches

Each major participant in the Center should supply a brief biographical sketch and selected bibliography (no more than 10 papers). Complete bibliographies may be required at the time of review but should not be included in the application.

13. Appendices

Certain points requiring detailed description may be placed in an appendix. Examples would be details of methodology, detailed protocols for clinical investigations, detailed plans for a demonstration program, or documentation of arrangements for collaborative efforts involving other institutions.

TIMETABLE

Pre-application meeting of potential applicants October 2, 1973.

Deadline for receipt of letters of intent November 1, 1973.

Deadline for receipt of applications January 15, 1974.

Notification of applicants regarding the decisions on applications, on or before June 1, 1974.